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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service • National Institutes of Health • National Cancer Institute

HE 20.3173/2:

PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. BLADDER TUMORS AMONG THE DOCK WORKERS OF GENOA (MEETING ABSTRACT).

Riccardo P, Marina V, Stefano B, Luca G, Federico V
No affiliation gives
Tumori; 67(2,SupplA):131 1981

An epidemiologic study carried out on dock workers in Genoa showed, among other things, an elevated mortality due to bladder tumors. This situation proved especially significant for certain work categories greatly afflicted with this type of tumor. Analysis of mortality taking into considerati on the period of exposure (assuming that the length of employment was indicative of this parameter) shows how a dose-effect relation between exposure and cancer development can be postulated. The bimodal course of these curves could lead to discussions of changes which have occurred in the work environment during the last 30 yr. (no Refs) (In ITA)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

2. SCLEROSING PERITUBULAR NODULES: A HEREDITARY RENAL ABNORMALITY IN VON RECKLINGHAUSEN'S DISEASE.

Mandybur TI, Weiss MA
Dept. Pathology and Lab. Medicine, Univ. Cincinnati Coll. Medicine, 231 Bethesda Ave., Cincinnati, OH, 45267
Hum Pathol; 12(8):704-712 1981

A previously unrecognized type of renal lesion characterized by the formation of multiple hamartomatous sclerosing peritubular nodules in the cortex is described. These lesions were hereditary, appearing in three members of a family, which included the mother and her two sons, in association with familial central von Recklinghausen's disease (bilateral acoustic schwannomas). The nodules originated as concentric peritubular proliferations of collagen producing spindle cells, which ultrastructurally showed myofibroblastic differentiation. Four stages of nodule development leading to progressive sclerosis and tubular destruction are described. In spite of widespread involvement of the cortex with numerous nodules, in none of the three patients was there any clinical manifestation of renal dysfunction or hypertension. (Author abstract) (13 Refs)

3. EPIDEMIOLOGY OF OCCUPATIONAL TUMORS OF THE URINARY TRACT (MEETING ABSTRACT).

Rubino GF, Piolatto G
Universita Torino, Via Zuretti 29, Turin, Italy
Tumori; 67(2,SupplA):131 1981

Italian and international observations concerning the incidence of urinary tract tumors in persons assigned to dye production have led us to conduct this analytical study aimed at identifying the carcinogenicity of specific amines and groups of amines. The causes of death of 906 workers in a local company for which they had detailed information on workers' activity in various departments were reviewed. 36 deaths due to urinary tract tumors were found as opposed to the 1.23 which would be expected on the basis of nationwide mortality. The excess was especially prominent among those assigned to benzidine and beta-naphthylamine production and to a lesser extent among those exposed by use or intermittent contact with them. In addition, an incidence approx 60x that expected was found among those assigned to the production of fuchsin and safranine T. Analysis of the processes involved in the chemical synthesis of these agents indicated that the agents responsible for the oncogenic action are probably o-toluidine and ditolylbase. The epidemiologic data in the literature on the human carcinogenicity of using the individual amines are revie wed. (no Refs) (In ITA)

4. RADIATION EFFECTS ON THE NORMAL BLADDER AND PROSTATE (MEETING ABSTRACT).

Howes AE, Bagshaw MA
Department of Radiology, Stanford University Medical Center, Stanford, CA
Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981

The bladder and prostate are frequently exposed to large doses of radiation in the treatment of pelvic malignancies. The early and late effects of radiation-induced bladder injury have been well documented for conventional forms of treatment, as tolerance of the organ is occasionally dose limiting, and reactions can be readily assessed and quantitated. These reactions and knowledge of dose-time-vol relationships will be discussed, together with more recent information concerning response to unconventional treatment techniques and the effect of chemical modifying agents. Radiation effects on the prostate gland are poorly documented and understood as they are rarely a significant clinical problem. However, careful analysis of large series of irradiated glands reveals significant changes in semen production, potency and urinary continence. The relative effects of external beam and interstitial irradiation techniques will be compared and the influence of radiobiological parameters will be discussed. (no Refs)

5. HELMINTHS IN THE INDUCTION OF CANCER. II. SCHISTOSOMA HAEMATOBIUM AND BLADDER CANCER.

Schwartz DA
Inst. Medicine, Far Eastern Univ., Manila, Philippines
Trop Geogr Med; 33(1):1-7 1981

Evidence that bilharzial infection plays an accessory, if not primary, role in bladder cancer induction is reviewed. Schistosoma haematobium infections are hyperendemic in Egypt, and bilharzial bladder cancer is the most prevalent cancer in Egyptian men. The bilharzial tumors differ greatly from nonbilharzial tumors in age and sex distribution, histopathology, and clinical presentation. The former are more common in men and greater than one-half of the patients are less than age 50. A characteristic feature of bilharzial bladder cancer is the great preponderance of squamous cell carcinoma, followed by transitional cell carcinoma, and adenocarcinoma, the tumors are always accompanied by pyogenic bacterial infection. Bladder tumors have been induced in monkeys and hamsters exposed to S haematobium cercariae, but more research is needed to define to the relationship between animal and human bilharzial tumors. The exact mechanism of bilharzial bladder carcinogenesis remains unknown. (45 Refs)

6. ON THE MUTAGENICITY OF NITROIMIDAZOLES.

Voogd CE
National Inst. of Public Health, P.O. Box 1, 3720 BA Bilthoven, The Netherlands
Mutat Res; 86(3):243-277 1981

The carcinogenic action of metronidazole in mice was reported in 1972. Since the n dimetridazole and ornidazole were shown to be carcinogenic in rats. Several 5-nitroimidazoles were carcinogenic to rats at 0.2% and mice at 0.15%. It is not certain whether the carcinogenicity is due to the catabolites formed by intestinal microorganisms or is caused by mammalian metabolism of these drugs under anaerobic conditions. The drug azathioprine (Imuran) was carcinogenic to mice, possibly caused bladder tumors within six yr in two patients (one received 255 g, the other 150 g) and lung adenocarcinoma in another case. The mercaptopurine group may have been responsible for these observations or the immunological surveillance may have been disturbed by the drug. The nitroimidazoles are indispensable drugs and as long as no other substitutes are available they should be used where it is appropriate, although some genetic damage and carcinogenic effect cannot be excluded. (160 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

7. RENAL TUMORS IN RATS TREATED WITH DIMETHYLNITROSAMINE AND/OR N-ETHYL-N-HYDROXYETHYLNITROSAMINE.

Kitahori Y, Ohshima M, Hiasa Y
First Dept. Pathology, Nara Medical Univ., Nara, Japan
Nara Igaku Zasshi; 32(2):181-188 1981

Male Wistar rats (4-5 wk old) were divided into seven groups; each group of rats were given one or both of two chemicals (dimethylnitrosamine, DMN, or N-ethyl-N-Hydroxyethylnitrosamine, NENH) mixed with standard food pellets during the first 2 wk of the experiment and then were given a stock die wk 3-36. Group 1 was fed 400 ppm DMN for wk 1 and a basal diet for wk 2; Group 2 was fed 400 ppm DMN wk 1 and 2; Group 3 was fed 100 ppm NEHN wk 1 and the basal diet wk 2; Group 4 was fed 1000 ppm NEHN wk 1 and 2; Group 5 was fed 400 DMN wk 1 and 1000 ppm NEHN wk 2; Group 6 was fed 1000 ppm NEHN wk 1 and 400 ppm DMN wk 2; Group 7 was fed the basal diet wk 1 and 2. Embryonal cell tumors were observed in 33% of the Group 1 rats, 85% of the Group 2 rats, and 8% of the Group 6 rats; no embryonal cell tumors were observed in the Group 5 rats. Renal cell tumors were observed in 16% of the Group 1 rats, 7% of the Group 2 rats, 38% of the Group 3 rats, 58% of the Group 4 rats, 33% of the Group 6 rats, and 30% of the Group 5 rats. (33 Refs) (In JPN)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

8. A PERMISSIVE ROLE OF THE PITUITARY IN ESTROGEN-INDUCED AND DEPENDENT RENAL TUMORS (MEETING ABSTRACT).

Lin YC, Loring JM, Villee CA
Department of Biological Chemistry and Laboratory of Human Reproduction, and Reproductive Biology Harvard Medical School, Boston, MA, 02115
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

Prolonged administration of estrogen by implanted pellets induces renal adenocarcinomas in hamsters. Many of these animals develop enlarged pituitaries with hyperplastic and neoplastic chan ges which occur especially in the pars intermedia. The pituitaries of the diethylstilbestrol (DES) implanted animals weigh 90-150 mg; those of control animals weigh 7-12 mg. The enlarged pituitaries have 9.7 x 10(-10) moles/mg protein of progesterone receptors compared to 0.75 x 10(-10) moles/mg protein in the controls. To determine whether some secretory product of the pituitary may play a role as a causative or permissive agent in renal tumorigenesis castrate male hamsters were hypophysectomized, implanted with DES pellets and tumors were transplanted under the kidney capsule two mo later. Eighty days later no tumors were evident in the kidneys of these animals. In the control series, castrate males were implanted with DES pellets and two mo later tumor tissue was transplanted under the kidney capsule. Between 60 and 85 days later seven of the eight controls had developed renal tumors. To determine the possible role of the pituitary in the primary induction of the kidney tumor, 35 castrate hypophysectomized hamsters were implanted with DES pellets. New pellets were implanted every three mo and the animals survived 12 to 15 mo. At autopsy not one of these animals had a tumor. Control castrate animals with the same schedule of pellet implantations all developed tumors within 12 mo. Hypophysectomized castrate animals implanted with DES pellets were injected either with a combination of follicle stimulating hormone and luteinizing hormone, one ug each per day, or with prolactin, one ug per day. A control group was injected with saline. These animals survived 12 to 15 mo but none developed kidney tumors. (no Refs)

9. EFFECT OF PHENOBARBITAL ON THE DEVELOPMENT OF NEOPLASTIC LESIONS IN THE LIVER OF CYCASIN-TREATED RATS.

Uchida E, Hirono I
Second Dept. Pathology, Nippon Medical Sch., Sendagi, 1-1-5, Bunkyo-ku, Tokyo 113, Japan
J Cancer Res Clin Oncol; 100(3):231-238 1981

The effect of phenobarbital (PHE) on neoplastic lesions induced in the liver and kidney of ACI rats by a single administration of cycasin (CYC) was investigated. Rats were placed into one of four groups: Group 1 received 100 mg CYC/kg by gavage and PHE at a level of 0.05% in their diet until the termination of the experiment; Group 2 received CYC alone; Group 3 received PHE alone; and Group 4 received no treatment. In Group 1, liver tumors were induced in 1/12 males and 7/12 females and one sarcoma and one interstitial tumor of the kidney were also induced. In Group 2, one liver tumor was found in a female, and two interstitial tumors of the kidney and one jejunal adenocarcinoma were induced. In Group 3, only one interstitial cell tumor in the testis was found. In Group 4,

two interstitial cell tumors in the testes, one pituitary adenoma, and one adrenocortical adenoma were found in males, and one pancreatic exocrine adenoma was found in a female. Significant numbers of gamma-glutamyl-transpeptidase (GGT)-positive foci were induced in Groups 1 and 3. In Group 2, a small number of tiny foci were seen. Many GGT-positive foci were observed in Group 4, however, they were small-sized. Thus, PHE possesses a tumor-promoting effect in terms of induction of neoplastic lesions in the liver, but not the kidney. (27 Refs)

10. CARCINOGENESIS AND AGING. I. MODIFYING EFFECTS OF AGING ON N-METHYL-N-NITROSOUREA-INDUCED CARCINOGENESIS IN FEMALE RATS.

Anisimov VN
Lab. Experimental Tumors, N. N. Petrov Res. Inst. Oncology, 68, Leningradskaya Str., Pesochny-2, Leningrad, 188646, USSR
Exp Pathol (Jena); 19(2):81-90 1981

Three- or 14-mo-old female rats were injected iv with N-nitroso-N-methylurea (MNU), 50 mg/kg body wt, 2 or 4x/wk. There was a direct correlation between the incidence of mammary carcinomas and MNU doses. Kidney tumors occurred inversely proportional to the dose of the carcinogen. Mammary adenocarcinomas were only observed in young MNU-treated rats. Cervicovaginal malignant tumors were only observed in old MNU-treated rats. The incidence of hematopoietic system tumors was the same in animals of both age groups. Rats treated with MNU showed acceleration of benign spontaneous tumor development. The effect of aging on the initial stage of MNU-induced carcinogenesis is believed to be determined by age-associated changes in the proliferative activity of target tissues. The effect of aging on the further development of carcinogenesis may be caused by age-associated hormonal, metabolic, and immunological shifts. (Author abstract) (42 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

11. PREDICTIVE VALUE OF THE DNA ALKALINE ELUTION TEST IN EVALUATING THE ONCOGENIC RISK FROM AROMATIC AMINES (MEETING ABSTRACT).

Bolognesi C, Cesarone CF, Santi L
Istituto Scientifico per lo Studio e la Cura dei Tumori, Genoa, Italy
Tumori; 67(2,SupplA):56 1981

The alkaline elution method was used to determine changes in the DNA molecule induced by aromatic amines with different chemical structures administered in vivo. The chemical compounds (benzidine, 1-naphthylamine and 2-naphthylamine, aniline, 2-nitroaniline, 2,4-dinitroaniline, o-toluidine and p-toluidine) were injected ip into male CDI Swiss mice in doses equivalent to 2/3 of the LD50. A significant increase in alkaline elutability of DNA was demonstrated 4 hr after administration in the liver and kidneys of animals treated with benzidine, 1-and 2-naphthylamine, o- and p-toluidine. A negligible increase in DNA fragmentation in alkali was found for aniline and 2-nitroaniline, while the av elution constant for 2,4-dinitroaniline falls within the range of the controls. The good correlation with the long-term carcinogenicity tests is especially significant for o- and p-toluidine, compounds only recently shown to be mutagens following broader investigations with particular systems of metabolic activation. The different physico-chemical properties and above all different mechanisms of biotransformation of these molecules in vivo characterize the different toxic and oncogenic properties of this class of compounds. The short-term tests of carcinogenesis are greatly limited by the difficulties of experimentally reproducing the same metabolic conditions which occur during the process of cellular neoplastic transformation. The alkaline elution test in vivo allows the normal metabolic pathways for chemical compounds and, in spite of the difficulties involved in extrapolating the results obtained with rodents to man, added to other information, such as chemical structure and level of environmental exposure, it enables definition of a correct toxicologic profile of chemical compounds. (no Refs) (In ITA)

12. INCREASED AMIDOPHOSPHORIBOSYLTRANSFERASE AND DECREASED XANTHINE OXIDASE ACTIVITY IN HUMAN AND RAT RENAL CELL CARCINOMA.

Prajda N, Donohue JP, Weber G
National Inst. Oncology, Budapest, Hungary
Life Sci; 29(8):853-860 1981

The behavior of the activity of the rate-limiting enzyme of the biosynthesis of purines, amidophosphoribosyltransferase (EC 2.4.2.14), and of the catabolism, xanthine oxidase (EC 1.2.3.2), was elucidated in primary renal cell carcinomas in human and in chemically-induced, transplantable renal cell carcinomas in rat. Enzyme activities were measured in the supernatant fluid prepared by centrifugation of 5% homogenates at 100,000 x g for 30 min. The activities in human and rat kidney for amidotransferase were 2.0 +-0.2 and 8.9 +-0.4 and for xanthine oxidase 0.4 +-0.09 and 5.5 +-0.3 umol per hr/per mg protein x 10(-2), respectively. In the human and rat tumors the activities of amidotransferase increased 1.5-to 2.7-fold and of xanthine oxidase decreased to 25 to 69% of those of the respective controls. The ratios of the activities of amidotransferase/xanthine oxidase were increased 2.1-and 5.3-fold in the tumors. Since amidotransferase activity increased and xanthine oxidase decreased in all examined kidney tumors, the alterations in the activities of these enzymes appeared to be linked with neoplastic transformation. With the reciprocal alterations in activity of the synthetic enzyme, amidotransferase, and the concurrent decrease in that of the catabolic enzyme, xanthine oxidase, the reprogramming of gene expression resulted in an imbalance that favors the synthetic over the degradative capacity. These results indicate the applicability of the pattern of enzymic imbalance discovered in rat hepatomas to human and rat kidney neoplasia. (Author abstract) (31 Refs)

13. METABOLIC FATE AND CARCINOGENICITY OF N-(OMEGA-HYDROXYALKYL)-N-(4 HYDROXYBUTYL)N ITROSAMINES, ANALOGS OF N-BUTYL-N-(4-HYDROXYBUTYL)NITROSAMINE, IN THE RAT.

Suzuki E, Takeda Y, Mochizuki M, Hashimoto Y, Okada M
Tokyo Biochemical Res. Inst., Takada 3-41-8, Toshima-ku, Tokyo 171, Japan
Gan; 72(4):539-546 1981

The metabolic fate and carcinogenicity of three omega-hydroxy derivatives of N-alkyl-N-(4-hydroxybutyl)nitrosamines, potent bladder carcinogens, were investigated in the rat. They were N-(2-hydroxyethyl)-N-(4-hydroxybutyl)nitrosamine (HEHBN), N-(3-hydroxypropyl)-N-(4-hydroxybutyl)nitrosamine (HPHBN), and N,N-bis(4-hydroxybutyl)nitrosamine (BHBN). The principal urinary metabolite of HEHBN as well as HPHBN was identified as the corresponding 3-carboxypropyl compound, while the main me-

tabolite of BHBN was N,N-bis(3-carboxypropyl)nitrosamine, indicating the preferential metabolic oxidation of the 4-hydroxybutyl chain to the 3-carboxypropyl group in the N-(omega-hydroxyalkyl)-N-(4-hydroxybutyl)nitrosamines. All three N-nitrosamines having the 4-hydroxybutyl chain induced neither bladder tumor nor any tumor in other organs under conditions similar to those used for N-alkyl-N-(4-hydroxybutyl)nitrosamines. The essential structural and metabolic requirements in N-nitrosamines for the induction of bladder cancer in the rat are discussed. (Author abstract) (25 Refs)

14. METABOLIC FATE OF N,N-DIPROPYLNITROSAMINE AND N,N-DIAMYLNITROSAMINE IN THE RAT, IN RELATION TO THEIR LACK OF CARCINOGENIC EFFECT ON THE URINARY BLADDER.

Suzuki E, Okada M
Tokyo Biochemical Res. Inst., Takada 3-41-8, Toshima-ku, Tokyo 171, Japan
Gan; 72(4):552-561 1981

The metabolic fate of N,N-dipropylnitrosamine (DPN) and N,N-dipentyl(=diamyl)nitrosamine (DAN), which induce tumors principally in the liver and esophagus but not in the urinary bladder, was studied in the rat, in order to elucidate the reason for this lack of carcinogenicity to the urinary bladder in contrast with the butyl homolog, N,N-dibutylnitrosamine (DBN), a potent bladder carcinogen. The principal urinary metabolite of DPN was identified as the omega-oxidation product N-propyl-N-(2-carboxyethyl)nitrosamine. The (omega-1)-oxidation product N-propyl-N-(2-hydroxypropyl)nitrosamine and its glucuronic acid conjugate were also characterized as metabolites. The principal urinary metabolite of DAN was N-amyl-N-(2-carboxyethyl)nitrosamine, which was formed by metabolic shortening of the amyl chain by omega- and beta-oxidations according to the Knoop mechanism. Besides this, seven compounds oxidized at omega-, (omega-1)-, (omega-2)-, and (omega-3)-positions of one or both amyl chains were isolated and characterized, some of which were shown to be also present as the corresponding glucuronide. The metabolic pattern of DPN and DAN was compared with that of DBN, and the lack of carcinogenicity of the former N-nitrosamines to the urinary bladder of rats is discussed on the basis of their urinary metabolites. (Author abstract) (20 Refs)

15. METABOLIC FATE OF N-BUTYL-N-(4-HYDROXYBUTYL)NITROSAMINE AND N,N-DIBUTYLNITROSAMINE IN THE GUINEA PIG, WITH REFERENCE TO THEIR CARCINOGENIC EFFECTS ON THE URINARY BLADDER.

Suzuki E, Aoki J, Okada M
Tokyo Biochemical Res. Inst., Takada 3-41-8, Toshima-ku, Tokyo 171, Japan
Gan; 72(4):547-551 1981

The metabolic fate of two urinary bladder carcinogens, N-butyl-N-(4-hydroxybutyl)nitrosamine(BBN) and N,N-dibutylnitrosamine (DBN), was studied in the guinea pig, in order to elucidate species differences of response to these N-nitrosamines in this animal species and the rat. Based on the urinary metabolites characterized after oral administration of these compounds, the metabolic pathways of BBN and DBN in the guinea pig were shown to be essentially similar to those in the rat. The principal urinary metabolite of BBN and DBN in the guinea pig, however, was not N-butyl-N-(3-carboxypropyl)nitrosamine (BCPN), as was the case in the rat, but the glucuronic acid conjugate of BBN and that of N-butyl-N-(3-hydroxybutyl)nitrosamine, respectively. The species variation in response to BBN and DBN as bladder carcinogens in these animals is discussed on the basis of the urinary excretion of BCPN. (Author abstract) (27 Refs)

16. THREE DIFFERENT HUMAN TUMOR CELL LINES CONTAIN DIFFERENT ONCOGENES.

Murray MJ, Shilo BZ, Shih C, Cowing D, Hsu HW, Weinberg RA
Center Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
Cell; 25(2):355-361 1981

We have obtained foci of transformed mouse cells after transfection of human DNA from colon and bladder carcinoma cell lines and a promyelocytic leukemia cell line. These foci can be shown to contain a large number of human DNA sequences by use of highly repetitive human DNA sequence probes. Cell DNA from primary foci can be used in a subsequent cycle of transfection resulting in secondary foci that contain relatively little human DNA. Secondary foci appear to contain only the human sequences proximal to those responsible for the transformed phenotype. A set of characteristic DNA restriction fragments is found in common among secondary foci derived from each tumor cell line DNA. Comparison of the common DNA fragments found in secondary foci derived from three different human tumor cell lines indicates that these three cell lines contain three different transforming genes. (Author abstract) (32 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

17. MULTIOCULAR CYST OF THE KIDNEY.

Meek JM, Bokinsky C, Edson M, O'Connell KJ, Kossow AS
Dept. Urology, Naval Regional Medical Center, Orlando, FL, 32813
South Med J; 74(8):931-935 1981

The case reports of three patients (a 55-yr-old woman, a 42-yr-old man, and a 21 -mo-old boy) with renal multiocular cysts are presented; and the presentation, diagnosis, etiology, and treatment of these benign lesions are discussed. Microscopically, the cysts in the two adults were lined by a single layer of flat epithelium. In the first patient, the tissue between the cysts contained fibroblasts and mature fibrous tissue without recognizable nephrons. In the second patient, the cysts were separated by a fibrous stroma with occasional small blood vessels and smooth muscle fibers. The lesion in the infant was composed of swirls and whorls of connecting tissue with focal nests of epithelial cells and numerous cystic structures. The initial diagnosis had been Wilms' tumor. Because of several cases of Wilms' tumor and renal cell carcinoma occurring in multiocular cysts and the difficulty of pre- or intraoperative diagnosis, nephrectomy is the treatment of choice. (20 Refs)

18. BEHAVIOR OF PRIMARY AND SERIALLY TRANSPLANTED ESTROGEN DEPENDENT RENAL CARCINOMA CELLS IN MONOLAYER AND COLLAGEN GEL CULTURE (MEETING ABSTRACT).

Talley DJ, Roy WA
Divisions of Biochemistry and Anatomy, Department of Basic Sciences, Marquette University Dental School, Milwaukee, WI, 53233
63rd Annual Meeting of the Endocrine Society, June 17-19, 1981, Cincinnati, Ohio. The Endocrine Society 385 pp., 1981.

The present study was undertaken to compare the behavior of isolated cells from primary and 1st-4th serially transplanted hormone-dependent tumors cultured either in monolayer or in collagen gels. Enzyme-dissociated cells from both estrogen-induced primary renal tumors in Syrian hamsters and from 1st-4th serially transplanted carcinomas contained similar progesterone receptor levels in culture. When cultured as monolayers in plastic flasks, isolated cells from primary tumors exhibited a marked decline in cell number after 4-6 days in culture. Monolayer-cultured cells from 1st and 2nd transplantation tumors remained essentially constant in cell number over a two wk culture period whereas cells from 3rd transplantation tumors underwent a 2-3 fold increase in cell number during two wk in culture. When primary tumor cells were cultured in collagen gels, the decline in cell number over a two wk period was prevented and progesterone receptor levels remained elevated. Neither cells from primary nor 1st transplantation tumors exhibited significant increases in cell number in collagen gels. Increasing the serum concentration of growth medium from 10% to 30% did not stimulate growth of cells under these conditions. Cells isolated from 4th transplantation tumors exhibited a 4-fold increase in cell number over a one-mo culture period whether cell were cultured as monolayers or in collagen gels. Progesterone receptor levels also remained elevated under both culture conditions. These data suggest that slow growing and well different iated renal tumors which are hormone dependent require a condition supplied by collagen gels for being maintained for long periods in culture. (no Refs)

19. THE EFFECT OF INTRAVESICAL THIO-TEPA AND MITOMYCIN C ON THE NORMAL BLADDER (MEETING ABSTRACT).

Soloway MS, Murphy WM
Department of Urology, University of Tennessee Center for Health Sciences, Memphis, TN
Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981

Increasingly intravesical chemotherapy is being utilized for both definitive therapy of superficial bladder tumors as well as prophylaxis following endoscopic resection or fulguration. Critical to the evaluation of the effect of intravesical chemotherapeutic agents on tumors is the ability to monitor urinary cytology. A series of experiments were designed to determine the effect of one of these drugs, thio-tepa (TTP) on the normal and abnormal mammalian urothelium. This model allows the comparison of the entire bladder with cytologic specimen obtained prior to cystectomy. The initial study analyzed the effect of thio-tepa or saline on the normal urothelium. One, 3, 7, and 22 days after a single instillation of TTP the exfoliated cells and the bladder were examined. There were no consistent morphologic differences between the treated and control groups. The same analysis was repeated after three weekly instillations of TTP with the same results. Thus, when cells having the cytologic appearance of neoplasia are found in the urine of a patient on TTP they should not be considered due to a 'thio-tepa effect' but as malignant. A similarly designed study examined the effect of Mitomycin C (MMC) on the normal bladder using these same parameters. Once again cellular degeneration and epithelial denudation was occasionally observed but drug related nuclear changes which might be confused with malignancy were rare. (no Refs)

20. SCANNING ELECTRON MICROSCOPY OF CYCLOPHOSPHAMIDE-INDUCED HYPERPLASIA OF THE RAT URINARY BLADDER (MEETING ABSTRACT).

Friedell GH
Saint Vincent Hospital, Worcester, MA
Long Term Normal Tissue Effects of Cancer Treatment, April 13-15, 1981, Bethesda, Maryland Committe for Radiation Oncology Studies; 1981

Urinary bladder damage caused by interperitoneally injected cyclophosphamide in male F344 rats was studied by light microscopy, scanning electron microscopy, and autoradiography. A dose response was evident in the number and size of lesions induced and the time of regeneration and repair. Scanning electron microscopy disclosed pleomorphic microvilli on the luminal surface of cells during the early phases of hyperplasia. The greatest number of cells with pleomorphic microvilli occurred 2, 5, and 7 to 8 days following injection of 75, 100, and 200 mg per kg of cyclophosphamide, respectively. Of the few rats surviving beyond 1 yr after a single injection, none had bladder lesions at any of the dose levels. The changes in the epithelium observed by scanning electron microscopy following cyclophosphamide injection were compared to those observed during bladder carcinogenesis. (no Refs)

21. THE APPARENT INHIBITION OF UROTHELIAL DNA SYNTHESIS IN NEONATAL RATS BY DIETARY SACCHARIN.

Lawson T, Hertzog P
Eppley Inst. Res. in Cancer, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Cancer Lett; 13(3):259-264 1981

The effect of sodium saccharin on urothelial cells was studied in Sprague-Dawley male and female rats. Parent rats were fed a diet containing 1%, 3%, 5%, and 7.5% saccharin. The females received the same diet during pregnancy and up to 21 days after birth. Significant differences in the body wt of the F1 males were only observed after 16 and 21 days in the group that derived from 7.5% saccharin-fed parents. Urothelial DNA synthesis was determined by the labeling index. The peak of DNA synthesis usually occurs between Day 0 and 2 after birth. In animals that derived from saccharin-fed parents the peak was decreased and delayed. Grain counts served as an indicator of 3H-thymidine incorporation into urothelial DNA. In the controls and the 1% saccharin-fed rats more than 80% of the cells showed greater than 11 grains. In the rats that derived from 3, 5, and 7.5% saccharin-fed parents 13.4%, 30.8%, and 14.4% urothelial cells contained greater than 11 grains, respectively. There is no explanation available for the different reaction of the 5%-saccharin group. In F0 rats, saccharin appears to be a non-genotoxic carcinogen and was excreted in the same amount as administered. In the present study the F1 rats showed saccharin-induced cellular changes which could be involved in carcinogenesis. (20 Refs)

22. EXPRESSION OF SILVER-STAINED NUCLEOLAR ORGANIZING REGIONS (AG-NORS) IN HUMAN CANCER.

Trent JM, Carlin DA, Davis JR
Dept. Internal Medicine, Cancer Center, Univ. Arizona, Tucson, AZ, 85724
Cytogenet Cell Genet; 30(1):31-38 1981

Five cases of ovarian adenocarcinoma, three cases of endometrial adenocarcinoma, and one case of transitional cell carcinoma of the bladder have been studied for expression of silver-stained nucleolar organizing regions (Ag-NORs). The modal chromosome number of these tumors varied from 37 to 72, with a wide range of chromosome numbers (13 to 150). The modal number of Ag-NORs in this sample varied from three to seven. Regression analysis among and between tumors demonstrated a proportionate increase in the number of Ag-NORs with increasing number of total chromosomes and increasing number of acrocentric chromosomes ($r = 0.64$ and 0.75, respectively). Modal assessment of Ag-NORs in both peripheral blood lymphocytes (PBLs) and cultured tumor cells in one patient revealed identical modes in normal and malignant cells. Also, no difference in the expression of Ag-NORs was observed between tumor cells obtained at biopsy and placed for 48 hr in agar culture and tumor cells established in finite monolayer culture. Our study provides further evidence for a proportionate increase in Ag-NORs with increasing numbers of acrocentric chromosomes and total chromosomes. (Author abstract) (22 Refs)

23. UNCONTROLLED NUCLEAR DIVISION: A MARKER OF ALTERED GROWTH CONTROL IN MSV-TRANSFORMED CELLS AND SEVERAL HUMAN TUMOR CELL LINES (MEETING ABSTRACT).

Somers KD, Murphey M
Department of Microbiology and Immunology, Eastern Virginia Medical School, Norfolk, VA
RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

CB blocks cytoplasmic division and normal cells respond by ceasing nuclear division resulting in the formation of predominately binucleate cells. In contrast, transformed cells exhibit uncontrolled nuclear division in the presence of cytochalasin B with the resultant multinucleate phenotype. We now report that normal rat kidney (NRK) cells transformed by a cold-sensitive (cs) mutant of MSV form colonies in soft agar and multinucleate in response to CB treatment equivalently at either the permissive or restrictive temperature, yet remain cs for maintenance of the morphological phenotype of transformation. Furthermore, cells grown at either temperature are tumorigenic in syngeneic rats. Similarly, morphological revertants of MSV-transformed NRK cells express many of the morphological and surface properties of normal cells, but form colonies in soft agar, multinucleate when treated with CB, and induce tumors in syngeneic rats. Taken together, these findings demonstrate that the morphological phenotype is dissociable from the growth or neoplastic phenotype of cell transformation. We have extended these studies to human tumor and normal cell cultures. Cell lines derived from melanoma, glioblastoma and carcinoma of the prostate, bladder, and kidney multinucleate in response to CB treatment whereas cell cultures derived from normal prostate, kidney, skin, lung, and other diseases remain binucleate under comparable conditions. These findings show that uncontrolled nuclear division is a common feature of several human tumor cell lines. (no Refs)

24. GENESIS OF PAPILLARY TUMOURS: HISTOLOGICAL AND MICROANGIOGRAPHIC STUDY.

Sarma KP
8 Mayfield Park South, Bristol BS16 3NG, England
Br J Urol; 53(3):228-236 1981

The technique developed to study the microangiography of healthy bladders has been applied to study the known vagaries of papillary tumors, their associated changes and their genesis. Epithelial hyperplasia (reactive hyperplasia), which develops as a form of mucosal self-defense, is a general, no nspecific tissue response to an adverse environment. The conversion of reactive hyperplasia into reactive autonomy represents the neoplastic process. The growth of abnormal arteries precedes the development of tumors. A papillary tumor results from a symbiotic growth relationship between such an abnormal artery and the overlying normal or hyperplastic epithelium. All known vagaries of papillary tumors have been studied. (Author abstract) (6 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

25. SPECIFIC RED CELL ADHERENCE: IMMUNOLOGIC EVALUATION OF RANDOM MUCOSAL BIOPSIES IN CARCINOMA OF THE BLADDER.

Stein BS, Reyes JM, Petersen RO, McNellis D, Kendall AR, Soloway MS
Dept. Urology, Temple Univ. Health Science Center, Philadelphia, PA
J Urol; 126(1):37-40 1981

We studied 103 random biopsies from patients with overt transitional cell carcinoma of the bladder for specific red cell adherence. We evaluated 62 random biopsies from patients whose primary tumors were positive for specific red cell adherence and 100% of the biopsies in these patients also were positive for specific red cell adherence regardless of the pathologic finding in the random biopsy. We evaluated 41 random biopsies from patients whose primary bladder tumors were negative for specific red cell adherence and only 27% of all biopsies in this group of patients were positive for specific red cell adherence. Thus, we found that in 92 of the 103 random biopsies (89%) the specific red cell adherence of the biopsy agreed with that of the primary tumor. The loss of red cell antigens in random biopsies that are histologically normal may prove to be the earliest measurable changes of the malignant potential of the urothelium. (Author abstract) (24 Refs)

26. PRACTICAL UTILITY OF SPECIFIC RED CELL ADHERENCE TEST IN BLADDER CANCER.

Catalona WJ
Jewish Hosp. St. Louis, 4960 Audubon Ave., St. Louis, MO, 63110
Urology; 18(2):113-117 1981

There is a highly significant correlation between specific red cell adherence (SRCA) tests for ABO(H) blood group antigens and the biologic potential of a bladder cancer in terms of both superficial tumor recurrences and the subsequent development of invasive cancer. The correlation with superficial recurrences is of limited practical value because almost one half of patients with antigen-positive tumors have superficial recurrences. Similarly, because in approx one third of patients with SRCA-negative tumors invasive cancer does not develop, SRCA tests

cannot be used to select patients for early cystectomy. Because invasive cancer proceeds to develop in less than 10% of patients with high-grade, antigen-positive tumors, SRCA tests may be of use to identify patients with high-grade tumors who deserve a trial of conservative therapy. SRCA tests must be interpreted with caution in patients who have been treated previously wi th radiation therapy or thiotepa, in whom false positive tests may occur, and in patients with type O blood in whom false negative tests may occur. (Author abstract) (11 Refs)

27. DETECTION OF ABH TISSUE ISOANTIGENS BY IMMUNOPEROXIDASE METHODS IN NORMAL AND NEOPLASTIC UROTHELIUM. COMPARISON WITH THE ERYTHROCYTE ADHERENCE METHOD.

Coon JS, Weinstein RS
Dept. Pathology, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL, 60612
Am J Clin Pathol; 76(2):163-171 1981

The expression of the ABH blood group antigens (BGAg) by carcinomas of the urinary bladder at the time of initial biopsy heralds a relatively benign clinical course, whereas antigen deletion in histologically similar tumors is often predictive of tumor recurrences and invasion. The use of BGAg as a tumor marker in the clinical setting has been limited by difficulties in demonstrating BGAg in tissue sections with the erythrocyte adherence test, especially for antigen H. In this study, immunoperoxidase methods were used to detect BGAg in deparaffinized tissue sections of normal and malignant human urothelium, and the results were compared with those of the erythrocyte adherence test performed on adjacent sections. Results with the two methods were similar for antigens A and B; however, a novel lectin-antilectin immunoperoxidase method was clearly superior for detecting antigen H. The immunoperoxidase method significantly reduced false-positive test results for antigen deletion in normal urothelium and more accurately predicted the subsequent clinical course in patients having urinary bladder cancer. (Author abstract) (32 Refs)

28. HLA ANTIGENS ON HUMAN TRANSITIONAL CELL CARCINOMAS (MEETING ABSTRACT).

O'Toole C
The London Hospital Medical College, University of London, London, England
Immunobiol; 159(1/2):189 1981

The expression of HLA-A and B series antigens has been compared on Transitional Cell Carcinomas (TCC) and lymphoid cells from the same patients. Lymphoid cells were typed by complement dependent cytotoxicity. Tumor cells were typed by antibody-dependent-cell-mediated-cytotoxicity (ADCC) in a 51 chromium isotope release method. The ADCC method proved sensitive, alloantisera were titrated to dilutions greater than or equal to 10(-3). TCC cells were typed after both short and long tissue culture; this ensured elimination of passenger cells. All HLA-A and B series antigens detected on the donor lymphocytes were also expressed on the tumor cells. However a strong anomalous reaction was observed on 6 out of 8 TCC with HLA-B14 antisera, while in no cases were the donor lymphoid cells reactive. This reaction was detected only on TCC; bladder fibroblasts from TCC patients were non reactive. Neoplastic cells of other histogenic origins, including a squamous cell carcinoma of bladder, did not react anomalously with HLA-B14 antisera. Cold targ et inhibition assays and absorption of HLA-B14 antisera with lymphoid cells from HLA-B14 donors indicated a strong competitive reactivity between the anomalous antigen on TCC cells and HLA-B14 on normal cells. Monoclonal antibody to B2 microglobulin competitively inhibited ADCC with anti HLA-B14 sera on target cells from B14 donors and TCC. These results show that human transitional cell carcinomas strongly express an HLA-B14-like antigen in addition to their normal HLA phenotype. (no Refs)

29. CLINICAL EVALUATION OF HUMAN CHORIONIC GONADOTROPIN (HCG), ALPHA-FETOPROTEIN (AFP), PROSTATIC SERUM ACID PHOSPHATASE (PSAP), CARCINOEMBRYONIC ANTIGEN (CEA) AND BETA-2-MICROGLOBULIN (B2MG) AS TUMOR MARKERS IN UROGENITAL MALIGNANCIES.

Kawamura J, Soeda A, Okada K, Yoshida O, Kosaka T, Nakajima K, Yoshi M, Morita R, Torizuka K
Dept. Urology, Faculty Medicine, Kyoto Univ., Kyoto, Japan
Hinyokika Kiyo; 27(3):269-278 1981

Serum hCG and AFP for testicular germ cell tumors, prostatic serum acid phosphatase (PSAP) for prostatic carcinoma, and serum CEA and B2MG for urogenital malignancies were measured by radioimmunoassay (RIA) techniques. A. Specific tumor marker: 1) hCG and AFP: AFP was detected in embryonal carcinoma (EC), infantile EC and teratocarcinoma (TC). AFP and/or hCG was detected in the mixed type of tumor consisting of EC, TC and choriocarcinoma. This was dependent on the major histological component of the tumor. Even in the pure seminoma, elevation of hCG was noted in 4 out of 17 cases, followed by normalization after orchiectomy. Alteration of AFP and hCG well demonstrated an effect of treatment and clinical courses. Reelevation of the markers revealed an advance of clinical staging and recurrence of the tumor. 2) PSAP: Serum levels of PSAP by RIA method correlated well with those by enzyme method but showed fewer pseudonegative values. Elevation of PSAP gave a clue to the initial diagnosis and to earlier detection of recurrence of prostatic carcinoma. B. Nonspecific tumor marker: 1) B2MG: Elevation of B2MG was seen in patients with advanced stage of urogenital malignancies. Such a rate of elevation was 62.5% in testicular carcinoma, 55.6% in renal cell carcinoma, 48.1% in bladder carcinoma, 45.5% in pelvic and ureteral tumors and 22.2% in prostatic carcinoma. B2MG increased in 46.9% of advanced urogenital cancers as a whole. 2) CEA: CEA was also elevated in the advanced stage of urogenital cancers, although its percentage was less than that in B2MG. Elevation of CEA was detected in 44.4% of prostatic carcinomas, 37.0% of bladder carcinomas, 36.4% of pelvic and ureteral tumors and 22.2% of renal cell carcinomas. No testicular carcinomas revealed an abnormal CEA value. 3) Combination of B2MG and/or CEA did not raise positive rates of the markers in each of the urogenital cancers. However, when these patients were divided into three groups such as 'alive' with disease and 'dead', according to the survival states, elevation of B2MG or B2MG and CEA was seen in patients in whom tumorous lesions were not eliminated or recurrence was noticed, indicating a poor prognosis. In conclusion, to estimate AFP and hCG or PSAP, as a specific tumor marker, and B2MG and/or CEA, as a nonspecific tumor marker, is a useful adjunct to detect clinical courses and to predict prognosis of urogenital malignancies. (28 Refs) (In JPN)

30. CARCINOEMBRYONIC ANTIGEN (CEA) IN PATIENTS WITH UROLOGIC CANCER. II. THE CLINICAL UTILITY OF PLASMA CEA AND URINARY CEA-LIKE SUBSTANCE IN UROTHELIAL CANCER.

Itoh M
Dept. Urology, Faculty Medicine, Kyoto Univ., Kyoto 606, Japan
Hinyokika Kiyo; 27(3):231-241 1981

Determinations were made of plasma CEA in 124 bladder cancer and 26 renal pelvic and ureteral cancer patients and also of urinary CEA in 86 bladder cancer patients by radioimmunoassay (zirconylphosphate-gel) with the following results. 1)Plasma CEA levels (mean +- SD) thus found were 2.4 +-1.6 ng/ml for normal subjects and 3.0 +-1.9 ng/ml for patients with benign urologic diseases. Patients with localized bladder cancer and those with metastasis gave respective values of 5.7 +-3.9 ng/ml and 10.7 +-8.1 ng/ml, which were significantly higher than a corresponding value for those with previous history of bladder cancer of 3.1 +-1.8 ng/ml (p less than 0.01). Of patients with renal pelvic and ureteral cancer, those with localized lesions gave a value of 6.0 +-6.0 ng/ml and those with metastasis showed a value of 13.8 +-9.9 ng/ml, the latter value being significantly higher than a corresponding value for those with previous history of renal pelvic and ureteral cancer of 3.6 +-2.4 ng/ml (p less than 0.05). 2) If cases showing plasma CEA levels of 6 ng/ml or above are regarded as CEA-positive, the positivity rates of plasma CEA in bladder cancer patients were 40.8% for the group with localized cancer and 67% for the group with metastasis; both figures were significantly higher than that for the group with previous history of bladder cancer, 7.6% (p less than 0.01). Among patients with renal pelvic and ureteral cancer, 38.5% of those with localized cancer and 71.4% of those with metastasis were positive for plasma CEA, with the latter figure being found to be significantly higher than a corresponding value for patients with previous history of renal pelvic and ureteral cancer of 16.7% (p less than 0.05). 3) Fifty-four bladder cancer patients who were followed up for more than 6 mo after operation were divided into two groups, with and without recurrence, and plasma CEA levels as determined before and 1 mo after operation were compared between the two groups. 4)Plasma CEA levels were further studied in relation to smoking habits. Urothelial cancer patients, regardless of whether smokers or nonsmokers, showed a significantly higher positivity rate of plasma CEA than benign disease patients (p less than 0.01). 5)Urinary CEA levels tended to be higher in females than in males. Even benign disease patients exhibited abnormally elevated urinary CEA levels in the presence of urinary tract infection, with a positivity rate in excess of 60%. 6) These results suggest that the plasma CEA as determined by immunoassay provides a useful means of assessing the efficacy of surgical treatment, determining the likelihood of recurrence and the presence or absence of metastasis and evaluating prognosis in patients with urothelial cancer. (23 Refs) (In JPN)

31. NATURALLY ARISING TUMORS OF THE INBRED WAB/NOT RAT STRAIN. II. IMMUNOGENICITY OF TRANSPLANTED TUMORS.

Middle JG, Embleton MJ
Dept. Chemical Pathology, Royal Liverpool Hosp., Prescot St., Liverpool, L7 8XP, England
JNCI; 67(3):637-643 1981

The immunogenicity of 28 transplanted naturally arising tumors of the inbred WAB/Not rat was investigated at early passages in strictly syngeneic, contemporary animals. Included were nephroblastomas, histologically benign and malignant mammary tumors, soft tissue and skin tumors, one lymphoid tumor, and two gastrointestinal lesions. In no case was evidence of immunogenicity observed when animals were treated with multiple grafts of irradiated (15,000 rad) tissue or by excision of a growing tumor. A few of these tumors were further investigated by other methods of immunization, including injection at various sites of irradiated cells followed by challenge at different sites and multiple injections of mitomycin C- or Formalin-treated cells. Again no evidence of immunogenicity was seen. Attempts to immunize with viable cells mixed with BCG or Corynebacterium parvum failed due to lack of tumor suppression by these agents. Limited concomitant immunity experiments yielded similarly negative results, except in one case of a fibrosarcoma for which a slight reduction in second tumor growth was observed when primary implants were very large. Some alterations in biologic properties during transplant passage and the incidence of post-excision recurrence and metastatic spread of some of the tumors are described. (Author abstract) (21 Refs)

32. LACK OF ASSOCIATION BETWEEN BK VIRUS AND EPENDYMOMAS, MALIGNANT TUMORS OF PANCREATIC ISLETS, OSTEOSARCOMAS AND OTHER HUMAN TUMORS.

Grossi MP, Meneguzzi G, Chenciner N, Corallini A, Poli F, Altavilla G, Alberti S, Milanesi G, Barbanti-Brodano G
Inst. Microbiology, Univ. Ferrara, Via Luigi Borsari 46, I-44100 Ferrara, Italy
Intervirology; 15(1):10-18 1981

BK virus (BKV) DNA sequences were not detected in 142 human tumors analyzed by DNA-DNA reassociation kinetics and blot hybridization. The investigation was focused mainly on those rare types of human tumors (ependymomas, choroid plexus papillomas, tumors of pancreatic islets and osteosarcomas) that are induced with highest frequency by BKV in experimental animals. In addition, other tumors of the urinary apparatus and of the CNS were analyzed. BKV tumor (T) antigen was not detected in neoplastic tissues, and BKV T antibodies were not found in sera and cerebrospinal fluids from patients with neoplasms. Sequences homologous to BKV DNA were found in normal tissue from a kidney carrying a carcinoma. The neoplastic tissue from the same organ, however, had no sequences homologous to BKV DNA. Such DNA does not belong to BKV but probably to another papovavirus related to BKV. (Author abstract) (30 Refs)

33. IDENTIFICATION OF THE POSSIBLE ONCOGENES INVOLVED IN DIFFERENT NEOPLASMS INDUCED BY AVIAN LEUKOSIS VIRUS (MEETING ABSTRACT).

Fung YK, Crittenden LB, Kung HJ, Fadly AM
Department of Biochemistry, Michigan State University, East Lansing, MI, 48824
RNA Tumor Viruses, May 20-24, 1981, Cold Spring Harbor, New York. Cold Spring Harbor Laboratory 294 pp., 1981.

Avian leukosis viruses (ALV) are known for their ability to induce lymphoid leukosis in young chickens. These viruses, however, are also able to induce a number of other neoplasms in chickens at a lower frequency. Since ALV genome does not appear to encode an oncogene, it was proposed that the viruses induce neoplastic transformation of the target cell by activation of a cellular oncogene. To examine this possibility, we have analyzed the ALV provirus structure in several different types of tumors induced by ALV. The results are consistent with the notion that viral DNA integrates next to a specific cellular 'oncogene' which then triggers a particular type of neoplastic

transformation. In the erythroblastosis tumor, we found that the ALV provirus is integrated next to the cellular sequences related to the oncogene of avian erythroblastosis virus (AEV). Avian myelocytomatosis virus (MC29) is capable of inducing nephroblastoma in chicks. In ALV induced nephroblastoma, we found the ALV provirus is linked to the cellular sequence related to the oncogene of MC29. We have demonstrated linkage of RAV-1 proviruses to the cellular sequences related to MC29 in most of the lymphoid bursal tumors. (no Refs)

34. NATURAL OCCURRENCE OF DELETION MUTANT OF HUMAN PAPOVAVIRUS BK CAPABLE OF INDUCING T ANTIGEN.

Watanabe S, Yoshiike K, Yuasa Y, Uchida S
Dept. Enteroviruses, Natl. Inst. Health, Kamiosaki, Shinagawa-ku, Tokyo, 141, Japan
J Gen Virol; 54(part2):431-435 1981

Human papovavirus BK DNA resistant to digestion with EcoRI endonuclease had the capacity to direct synthesis of T antigen in human embryonic kidney cells. The study demonstrated the natural occurrence of defective deletion mutants with intact early functions of the viral genome. (Author abstract) (17 Refs)

REVIEWS AND OTHER RELATED STUDIES

35. ANTIBODIES TO CARCINOGENS-DNA ADDUCTS.

Poirier MC
Lab. Experimental Pathology, NCI, NIH, Bethesda, MD, 20205
JNCI; 67(3):515-519 1981

The preparation of rabbit antibodies to carcinogen-DNA adducts, the sensitivity and specificity of the antibodies, and their uses in studying carcinogen binding in rat tissues and cell cultures are reviewed. Among the areas currently under investigation by radioimmunoassay are the nature and extent of carcinogen binding to liver and kidney DNA in rats fed 2-acetylaminofluorene and the determination and manipulation of DNA adducts in cultured cells exposed to N-acetoxy-2-acetylaminofluorene. Solid-phase immunoassays may make it possible to measure adducts in a single cells, and direct visualization of adducts on DNA by electron microscopy may enable the localization of a carcinogen with respect to proximity of single-strand gaps, repair patches, or replication complexes. (11 Refs)

36. ENDOGENOUS CARCINOGENS.

Hill MJ
Bacterial Metabolism Res. Lab., Central Public Health Lab., London, England
Practitioner; 225(1356):803-804,807-809 1981

Estradiol is a potential endogenous carcinogen. Consuming a high fat/high energy diet, by increasing circulating estrogen levels and estrogen receptor activity, may increase the risk of carcinogenesis in estrogen-dependent tissues (breast, endometrium, possibly ovary). The role of of cholesterol in carcinogenesis is not yet clear. The author's studies showed no relationship between fecal cholesterol levels and the risk of intestinal cancer in case-control studies. Some of the numerous urinary metabolites of tryptophan seem to be related to non-industrial bladder cancer. Intestinal bacteria can derive carcinogenic substances (ethionine, phenol, p-cresol, N-nitroso compounds, bile acid metabolites, etc) from dietary components and convert exogenous chemicals (eg, polycyclic aromatic hydrocarbons) to proximate carcinogens. It is relatively easy to determine which carcinogens might be produced under ideal conditions, but there is limited information on which carcinogens are actually produced in vivo, and very little information regarding their importance. (27 Refs)

37. CANCER RESEARCH IN EAST AFRICA.

Ziegler JL
NCI, Bethesda, MD
Bull Am Coll Surg; 66(6):14-16 1981

The Makerere University Medical School of Kampala, Uganda is conducting research on the epidemiology and treatment of Burkitt's lymphoma, malignant melanoma (which develops only in the unpigmented skin of black Africans), hepatocellular carcinoma, and Kaposi's sarcoma, the chemotherapy of Hodgkin's disease, serologic surveys of patients with the tropical splenomegaly syndrome, the chemoprevention of skin cancer in African albinos, the epidemiology of Buruli ulcer (caused by a cold-growing mycobacteriu m), and the treatment and prevention of bladder carcinoma in areas of endemic bilharziasis. (no Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. THE GENETIC TOXICOLOGY OF ALDRIN AND DIELDRIN.
Ashwood-Smith MJ
Environmeata' Toxicology Res. Group, Dept. Biology, Univ. Victoria, Victoria, BC V8W 2Y2, Canada
Mutat Res; 86(2):137-154 1981

RADIATION CARCINOGENESIS

2. EFFECTS OF LOW-LEVEL RADIATION ON BIOLOGIC SYSTEMS: A LITERATURE REVIEW.
Best TL, Hoditschek B
Eastern New Mexico Univ., Portales, NM
Effects of Low-Level Radiation on Biologic Systems: A Literature Review. Available from National Technical Information Service, Springfield, VA, as SAND-80-7143:, 246 pp., 1981.

3. PHOTOCARCINOGENESIS: AN OVERVIEW.
Forbes PD
Skin and Cancer Hosp., 3322 North Broad St., Philadelphia, PA, 19140
J Invest Dermatol; 77(1):139-143 1981

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4. EPIDEMIOLOGICAL CORRELATIONS BETWEEN DIET AND CANCER FREQUENCY.
Correa P
Louisiana State Univ. Medical Center, New Orleans, LA, 70112
Cancer Res; 41(9,part2):3685-3689 1981

5. ROLE OF DIETARY FIBER IN DIVERTICULAR DISEASE AND COLON CANCER.
Talbot JM
Life Sciences Res. Office, Federation of American Societies for Experimental Biology, Bethesda, MD, 20014
Fed Proc; 40(9):2337-2342 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

6. PRIMARY HEPATIC CANCER IN ALCOHOLICS.
Tamburro CH, Lee HM
Liver Res. Center, Div. Digestive Diseases and Nutrition, Univ. Louisville Health Sciences Center, 511 South Floyd St., Louisville, KY, 40232
Clin Gastroenterol; 10(2):457-477 1981

7. PANCREATIC CANCER AND ALCOHOL.
Okuda K, Ohnishi K
Dept. Medicine, Chiba Univ. Sch. Medicine, 1-8-1 Inohana, Chiba City (280), Japan
Clin Gastroenterol; 10(2):479-484 1981

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Trop Geogr Med; 33(1):1-7 1981

9. GENETICS OF WILMS'S TUMOR.
Matsunaga E
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Hum Genet; 57(3):231-246 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

10. NEOPLASMS: COMPARATIVE PATHOLOGY OF GROWTH IN ANIMALS, PLANTS, AND MAN.
Kaiser HE
Dept. Pathology, Univ. Maryland Sch. Medicine, Baltimore, MD
Neoplasms: Comparative Pathology of Growth in Animals, Plants, and Man. Baltimore, Williams and Wilkins, 908 pp., 1981.

11. PULMONARY CARCINOGENESIS. ARYL HYDROCARBON HYDROXYLASE.
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Dept. Medicine, Baylor Coll. Medicine, Houston, TX, 77030
Cancer Treat Res; 1:1-34 1981

12. THE GENETIC TOXICITY OF HYDROXYLAMINES.
Marley P, Robinson E
Dept. Biological Sciences, State Univ. New York at Albany, Albany, NY, 12222
Mutat Res; 86(2):155-191 1981

MODIFICATION OF CARCINOGENESIS

13. MODIFYING FACTORS OF CHEMICAL CARCINOGENESIS.
Beliaev II, Litvinov IuA
Medical Inst., Gorki, USSR
Gig Sanit; (6):59-62 1981
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14. ANTIPROLIFERATIVE EFFECTS OF RETINOIDS RELATED TO THE CELL CYCLE-SPECIFIC INHIBITION OF ORNITHINE DECARBOXYLASE.
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Dept. Pharmacology, Univ. Arizona Coll. Medicine, Tucson, AZ, 85724
Ann NY Acad Sci; 359:281-297 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

15. PATHOGENESIS OF THYMIC LYMPHOMAS IN C57BL MICE.
Beniver J
Laboratoire d'Anatomie Pathologique, Tour de Pathologie B. 23, Universite de Liege au Sart Tilman, 4000 Liege, Belgium
Pathol Res Pract; 171(2):268-278 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

16. CRITICAL ASSESSMENT OF THE VALUE OF IN VITRO CELL TRANSFORMATION FOR PREDICTING IN VIVO CARCINOGENICITY OF CHEMICALS.
Brookes P
(c/o Lohman, P. H.), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 86(2):233-242 1981

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17. MAMMALIAN GENETICS AND CANCER.
Russell ES
Jackson Lab., Bar Harbor, ME, 04609
Prog Clin Biol Res 45: 327 pp., 1981.

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. EPIDEMIOLOGY OF CANCER.

Pawlega J
Pracownia Epidemiologii, Oddzial Instytutu Onkologii w Krakowie, ul. Garncarska 11, 31-115 Krakow, Poland
Przegl Lek; 38(5):447-451 1981

Cancer epidemiological data are presented for Krakow (urban area) and a nearby rural area for the period from 1965 on the basis of Cancer Registry data. The overall standardized cancer morbidity (per 100,000 population) in men in Krakow was 285 (70.9 for lung cancer, 35.1 for gastric cancer, 22.9 fo r skin cancer, 12.3 for pancreatic cancer, and 11.0% for urinary bladder cancer). The overall cancer mortality for men in the rural area was 177.1 (38.9 for lung cancer, 33.1 for gastric cancer, 9.6 for kin cancer, 8.3 for prostate cancer, and 8.0 for urinary bladder cancer). The cancer morbidity for women in Krakow was 201.1 (37.7 for breast cancer, 22.0 for cancer of the uterine cervix, 14.8 for gastric cancer, 14.9 for skin cancer, and 12.7 for lung cancer). The corresponding figures for the rural women were 122.1 (overall morbidity); 17.2 for gastric cancer, 17.8 for breast cancer. The percentage of cases diagnosed histologically was higher among the urban than among the rural patients, and the percentage of the patients not receiving antitumor therapy was higher among the latter. The relative 5-yr survival rates in men were higher among the urban patients than among the rural ones for all major localizations (lips, stomach, rectum, larynx, lungs, prostate, and bladder) except skin cancer, and the relative 5-yr survival of the urban women was higher for all major localizations (cancer of the stomach, skin, breasts, uterine cervix, endometrium, ovaries, and leukemia). (16 Refs) (In POL)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

2. A CASE-CONTROL STUDY OF BLADDER CANCER IN THE UNITED STATES RUBBER AND TYRE INDUSTRY.

Checkowway H, Smith AH, McMichael AJ, Jones FS, Monson RR, Tyroler HA
Occupational Health Studies Group, Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27514
Br J Ind Med; 38(3):240-246 1981

A case-control study of bladder cancer was conducted in five United States rubber and tire companies to determine if there were high-risk jobs and work areas within the industry. The study included 220 male cases of bladder cancer, of whom 107 were identified from hospital record reviews and 113 from death certificates. Each case was matched individually with two industry controls by sex, race, yr of birth, and company. One control was matched additionally by yr of hire and duration of employment. Comparisons of cases and controls not matched by yr of hire and age of hire showed no differences for those variables, which suggests that age and calendar period of first exposure to the industry were not risk determinants. When the work histories of both cases and controls were contrasted it was found that cases were more likely than controls to have worked in milling (odds ratio (OR) = 1.91) and calender operation (OR = 2.21) jobs. The relative risk estimates for milling and calender operation both exhibited linear trends of increase with duration of exposure. Milling and calender operation jobs entail potential exposures to volatilized reaction products from heated rubber stock. A better understanding of etiological associations with job type will require more detailed characterization of the work environment with regard to the sources and levels of aromatic amines and other suspected bladder carcinogens. (Author abstract) (25 Refs)

3. SOURCE OF DRINKING WATER AT HOME AND SITE-SPECIFIC CANCER INCIDENCE IN WASHINGTON COUNTY, MARYLAND.

Wilkins JR, Comstock GW
Dept. Preventive Medicine, Ohio State Univ., 410 West Tenth Ave., Columbus, OH, 43210
Am J Epidemiol; 114(2):178-190 1981

A nonconcurrent prospective study was conducted to investigate the postulated relationship between organic chemical by-products of water chlorination and risk of human cancer. Vital records and nonofficial census data available for each of nearly 31,000 study subjects were used to compute selected sex- and site-specific cancer incidence rates in a well-defined county population. Age, socioeconomic status, smoking history, source of drinking water at home, and other individual characteristics of the study population were examined in relation to the cancer rates. The drinking water source variable consisted of three historical cohorts, each distinguished by a different degree of exposure to chloroform and other chlorination by-products. Incidence rates for cancer of the bladder among men and for cancer of the liver among women were nearly twofold higher in the drinking water cohort that had been supplied chlorinated surface water at home when compared to the cohort with a history of consumption of unchlorinated ground water. The differences, however, were not statistically significant. A complementary mortality study also suggested an association of chlorinated water with cancer of the liver and urinary tract. The findings in Washington County indicate the need for further studies of individuals with different histories of exposure to chlorinated and unchlorinated drinking water. (Author abstract) (49 Refs)

4. BLADDER CANCER IN PET DOGS: A SENTINEL FOR ENVIRONMENTAL CANCER?

Hayes HM, Hoover R, Tarone RE
Environmental Epidemiology Branch, NCI, NIH, 3C07 Landow Bldg., Bethesda, MD, 20205
Am J Epidemiol; 114(2):229-233 1981

Proportional morbidity ratios (PMRs) were calculated for cancers, by site or type, in 8,760 pet dogs seen at 13 veterinary medical teaching hospitals in the United States and Canada. A significant positive correlation was seen between the PMRs for canine bladder cancer and the overall level of industrial activity in the host county of the hospital. An analysis of mortality from bladder cancer among white men and women in the same US counties showed similar correlations with industrial activity. Canine bladder cancer could be a sentinel condition whose investigation in certain locales might lead to early identification of carcinogenic hazards in the general environment. (Author abstract) (14 Refs)

5. CANCER RISK IN PESTICIDE-EXPOSED AGRICULTURAL WORKERS.

Barthel E
Bezirksfachkrankenhaus fur Lungenkrankheiten und Tuberkulose, Amsee 1, DDR-2060 Waren (Muritz), E. Germany
Arch Geschwulstforsch; 51(7):579-585 1981

Cancer risk was studied in 1,658 agricultural workers who had been exposed to pesticides for at least 5 yr in a cohort study. Malignant tumors were found in 169/1,658 cases; the tumors were confirmed histologically in 124/169 cases. Tumors of the esophagus, nasal cavity, soft tissues, lymphoid tissue, skin melanoma, lymphosarcoma, and lymphocytic leukemia were diagnosed in 1 case each. Other tumors included stomach in 21 cases, rectum in 7, liver in 2, gallbladder in 2, pancreas in 7, larynx in 4, trachea, bronchi, and lungs in 59, skin in 19, prostate in 11, penis in 2, urinary bladder in 7, brain in 2, and thyroid gland in 2. Lymphogranulomatosis was diagnosed in two cases, plasmocytoma in three, and myeloid leukemia in two. The difference between the exposed group and general epidemiological data was significant for lung cancer only (50 cases among exposed patients from 1970-1978 versus an expected value of 27.5). The av length of exposure of the lung cancer patients was 13.6 yr (6-23 yr), and the av latent period was 17.5 yr (6-29 yr). The higher incidence was not related to smoking habits, which suggests the etiological role of pesticide exposure. Based on intraindividual exposure data, experimental data, and on the use of pesticides in East Germany, the pesticides of greatest concern are arsenic-containing compounds, dicophane (DDT), lindane, and phenoxy acids. (21 Refs) (In GER)

6. EPIDEMIOLOGICAL STUDIES INTO THE POSSIBLE CARCINOGENICITY OF HAIR DYES.

Clemmesen J
(c/o P. Lohman), Medical Biological Lab. TNO., P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 87(1):65-79 1981

Epidemiological studies of the carcinogenicity of hair dyes are complicated by (1) too broad a definition of occupation, with hazards to specific job categories being overlooked, and too narrow a definition, making the surveyed group too small to yield significant results, (2) exposure to competing or cooperating carcinogens, (3) uncertain influence of life style, (4) latency period and changes in occupation, and (5) changes and regional variations in occupational classification. A review of reports on cancer incidence among barbers, hairdressers, and their customers is made with respect to urinary bladder, lung, larynx, and breast. The evidence is still apparently insufficient to support a link between exposure to hair dye and cancer. Further research with more statistically valid sampling is recommended. (30 Refs)

7. URINARY EXCRETION OF TRYPTOPHAN METABOLITES IN ISONIACID- AND PHTHIVAZID-TREATED PATIENTS.

Martynenko AG, Kartasheva LA, Aberun DE
R. E. Kavetsky Inst. of Problems of Oncology, Acad. Sciences Ukranian SSR, Kiev, USSR
Vop9 Onkol; 27(7):43-47 1981

The levels of tryptophan metabolites in the urine of 30 isoniacid- and phthivazid-treated patients with tuberculosis and 25 healthy subjects were determined by paper chromatography. The urine of healthy subjects was found to contain tryptophan, indican, tryptamine and urea, while that of tuberculosis patients contains tryptophan metabolites, including 3-hydroxykynurenine, known as carcinogen. Administration of pyridoxine does not eliminate metabolic disturbances caused by anti-tuberculosis preparations, while thiamine may inhibit pyridoxine enzymes, thus aggravating these disorders. (Author abstract) (31 Refs) (In RUS)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

8. CARCINOGENESIS IN SYRIAN HAMSTERS BY N-NITROSO-2,6-DIMETHYLMORPHOLINE, ITS CIS AND TRANS ISOMERS, AN THE EFFECT OF DEUTERIUM LABELING.

Rao MS, Scarpelli DG, Lijinsky W
Dept. Pathology, Northwestern Univ. Medical Sch., 303 East Chicago Ave., Chicago, IL, 60611
Carcinogenesis; 2(8):731-735 1981

Syrian golden hamsters were divided into groups of 20 each. They were given doses of N-nitroso-2,6-dimethylmorpholine (NDMM), its cis or trans isomer, or its alpha-d4 or beta-d2 deuterium-labeled derivatives. The weekly doses (mg/kg body wt) were NDMM 18 or 50; cis-NDMM 11.5 or 31; trans-NDMM 6.5 or 17; d4 18 or 50; d2 50. A total of 52 benign and 21 malignant tumors resulted, most associated with the pancreas, liver, respiratory system, and kidneys. The survival rate among hamsters treated with cis-NDMM was about the same as the rate for those treated with NDMM. The survival rate with trans-NDMM was higher, indicating that trans-NDMM was a less potent carcinogen. Treatment with d4 produced tumors earlier than treatment with d2, suggesting that d4 was the more potent of the two. The overall incidences of malignant tumors for the NDMM, d4, and d2 groups were not significantly different. Activation to mutagenicity by pancreas microsomes, and binding to DNA of the pancreas did not differ between the isomers. (21 Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

9. HORMONAL INDUCTION OF KIDNEY TUMOURS IN MALE HAMSTERS. INHIBITION OF GROWTH BY A PHENOTHIAZINE DERIVATIVE (PERPHENAZINE).

Saluja PG, Hamilton JM, Thody AJ
Dept. Anatomy, Sch. Medicine, Aberdeen, Scotland
Eur J Cancer Clin Oncol; 17(7):767-773 1981

Experiments have shown that long-term treatment of male hamsters with estrogen will cause renal carcinomas, neoplastic changes in the pars intermedia of the pituitary and highly elevated levels of melanocyte-stimulating hormone (MSH). To test if MSH was fundamentally involved in renal carcinogenesis, a group of hamsters was treated for 317 days with perphenazine which is known to elevate MSH levels. A second group was treated with estrogen while a third received a combination of estrogen and perphenazine for a similar period of time. Serum MSH levels were significantly elevated in the perphenazine group but kidney tumors were absent. All estrogen-treated animals developed kidney tumors but only 19% of those given the combined treatment developed kidney tumors despite

highly elevated levels of MSH. The findings suggest that MSH does not play a significant role in renal carcinogenesis in the hamster. Perphenazine may inhibit the induction of estrogen-induced tumors by competing with estrogen for receptors in the kidney or may protect cells from toxic injury by stabilizing cell and microsomal membranes. The phenothiazines are known to induce, and increase the activity of, microsomal enzymes and that may lead to enhanced detoxification of the carcinogen. Other effects of phenothiazines include elevation of prolactin levels. The fact that the body wt of animals treated with DES and perphenazine was significantly lower than that of the other groups may indicate that the reduction in tumor incidence was the result of a certain degree of undernutrition. Further work is required to elucidate the mechanism of tumor inhibition by phenothiazine derivatives. (Author abstract) (32 Refs)

10. EFFECTS OF CHLOROFORM AND DIMETHYLNITROSAMINE ON RENAL CARCINOGENESIS IN UNILATERALLY NEPHRECTOMIZED RATS FED FORMIC ACID 2-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]HYDRAZIDE.

Hirose M, Imaida K, Ito H, Hayashi M, Ishihara Y, Ito N
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
Carcinogenesis; 2(8):703-708 1981

Male Fischer rats were divided into five groups. Group 1 was subjected to unilateral nephrectomy (UN). After 2 days dimethylnitrosamine (DMN: 20 mg/kg body wt) was injected ip. One wk after UN the rats were placed on a diet containing O.2% 2-[4-(5-nitro-2-furyl)thiazolyl]hydrazide (FNT). Two wk after UN they received CHCl3 (400 mg/kg body wt). Group 2 received the same treatment without the FNT diet. Group 3 received the same treatment as group 1, except that CHCl3 treatment came before UN. Group 4 received the same treatment as group 3, but without FNT. Group 5 received only the FNT diet. Rats from each group were studied at 8, 16, and 32 wk. Renal tubular hypertrophy was found in 100% of groups 1, 3, and 5 at all three times. Tubular hyperplasia was found in group 1 (0%, 53.3%, 100%), group 3 (20%, 52.9%, 94.4%) and group 5 (0%, 0%, 94.1%) at 8, 16, and 32 wk, respectively. Renal cell tumors were found at 32 wk in groups 1 (85%), 3 (88.9%), and 5 (17.6%). No tumors were found in groups 2 and 4. The results from groups 2 and 4 show little or no initiating effect for FNT. Slight enhancement of renal tumors was produced by UN. The results from groups 1 and 3 indicate that UN and CHCl3 treatments had about equal effect in inducing preneop lastic changes in rat kidney. The enhancement of tubular hyperplasia and renal cell tumors by combined treatment with CHCl3, DMN, UN, and FNT in the initiating and promoting stages was confirmed. (22 Refs)

11. MODIFICATION OF THE MUTAGENICITY AND TERATOGENICITY OF CYCLOPHOSPHAMIDE IN RATS WITH INDUCERS OF THE CYTOCHROMES P-450.

Hales BF
Dept. Pharmacology and Therapeutics, McGill Univ., Montreal, Quebec H3G 1Y6, Canada
Teratology; 24(1):1-11 1981

The chemotherapeutic agent cyclophosphamide (CP) may act as a carcinogen if it is enzymatically metabolized to reactive intermediates with alkylating, mutagenic, or cytotoxic effects, which activation is thought to be catalyzed by the cytochrome P-450 monooxygenase system. Phenobarbital (PB) induces the hepatic cytochrome P-450 that is involved in the activation of CP to both alkylating and mutagenic metabolites; beta-naphthoflavone (bNF) induces a different cytochrome P-450 and actually decreases the activation of CP by liver microsomes. Using rats pretreated with either PB or bNF, the activation of CP to mutagenic metabolites by enzyme fractions on day 13 of gestation was measured with the Ames test on Salmonella typhimurium TA1535 and teratogenicity was assessed in vivo by treatment of rats with CP on day 13 of gestation. CP was activated to mutagenic metabolites to the same extent (on a tissue wet wt basis) by enzyme fractions from maternal liver, kidney, and placenta, despite differences in cytochrome P-450 content, but fetal homogenates did not activate CP. PB pretreatment increased the liver cytochrome P-450 content 1.8-fold and the activation of CP by maternal liver microsomes 10-fold; however, PB did not alter the activation of CP by maternal kidney, by placenta, or by the fetus. PB pretreatment increased the teratogenicity of CP as measured by an increased incidence of malformed embryos or by decreased fetal wt. Pretreatment with bNF did not induce the hepatic cytochrome P-450 in the pregnant rat; did not change the activation of CP to mutagenic metabolites by liver, kidney, the placenta, or the fetus; and had no effect or decreased the teratogenicity of CP. These results suggest that the mother, rather than the fetus, is the site of PB activation; that the principal site of activation is the maternal liver; and that there is a correlation between the teratogenicity and mutagenicity of CP after induction by cytochrome P-450. (36 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

12. IN VIVO KINETICS OF O(6)-METHYLGUANINE AND 7-METHYLGUANINE FORMATION AND PERSISTENCE IN DNA OF RATS TREATED WITH SYMMETRICAL DIMETHYLHYDRAZINE.

Herron DC, Shank RC
(c/o Shank) Dept. Community and Environmental Medicine, Univ. California Coll. Medicine, Irvine, CA, 92717
Cancer Res; 41(10):3967-3972 1981

The rates of appearance and removal of 7-methylguanine and O6-methylguanine in DNA from rat liver, kidney, and colon were determined at various intervals up to 120 hr after ip administration of 10.2, 40.7, 81.5, or 163 mg 1,2-dimethylhydrazine (SDMH) per kg body wt (1/16, 1/4, 1/2, or 1 50% lethal dose) using high-pressure liquid chromatography and fluorescence spectrophotometry. In most cases, increasing doses of SDMH slowed the rate of methylation of DNA, especially of the liver; colon DNA was methylated at a faster rate than was liver DNA, and kidney DNA was methylated at the slowest rate following SDMH administration. Removal of O6-methylguanine was slow (half-life, 37 to 50 hr) when this base was present in liver DNA at concentrations above 400 umol/mol guanine; as the concentration fell below 300 umol O6-methylguanine per mol guanine, the removal rate more than doubled (half-life, 16 to 19 hr). Some evidence was obtained to suggest that in the first 12 hr after max DNA methylation following SDMH administration, a rapid time-dependent removal of 7-methylguanine from liver and kidney but not colon DNA occurred. In these instances, then, the rates of formation and removal of aberrant methylated bases did not follow first-order kinetics. (Author abstract) (33 Refs)

13. DIFFERENTIATION OF THE MECHANISMS OF ONCOGENICITY OF 1,4-DIOXANE AND 1,3-HEXACHLOROBUTADIENE IN THE RAT.

Stott WT, Quast JF, Watanabe PG
Toxicology Res. Lab., Dow Chemical U.S.A., Midland, MI, 48640
Toxicol Appl Pharmacol; 60(2):287-300 1981

Two tumorigenic agents, 1,4-dioxane (DX) and 1,3-hexachlorobutadiene (HCBD) were compared to the known mutagen dimethylnitrosamine (DMN) to determine whether their actions were by a genetic or nongenetic mechanism. Male Sprague Dawley rats were given tumorigenic doses of DX in drinking water (0, 10 or 100 mg/kg/day for 11 wk), HCBD by gavage (0, 0.2, or 20 mg/kg/day for 3 wk), or DMN by gavage (3 mg/kg/day for 3 wk). Other groups of rats were given single doses of DX (10, 100, 1,000 mg/kg), HCBD (0.2, 20 mg/kg), or DMN (3 mg/kg) by gavage. DX produced no genotoxic effects at tumorigenic doses. A single large dose produced no alkylation of DNA or increase in DNA repair. Repeated high doses of DX were hepatotoxic. HCBD produced a minor genotoxic effect compared with DMN. DNA repair in renal tissue was increased 1.27-1.54-fold by HCBD (20 mg/kg); DNA alkylations occurred at the rate of 0.78 per 10(6) nucleotides. No mutations were produced in the Ames' bacterial mutagenesis assay. HCBD produced renal cytotoxicity. Apparently DX induces tumors by a nongenetic mechanism. HCBD acts primarily in a nongenetic way, but is weakly genotoxic. Risk from either compound is likely only at cytotoxic doses. (34 Refs)

14. METABOLISM OF CHEMICAL CARCINOGENS BY CULTURED HUMAN AND RAT BLADDER EPITHELIAL CELLS.

Autrup H, Grafstrom RC, Christensen B, Kieler J
Lab. Environmental Carcinogenesis, Copenhagen, Denmark
Carcinogenesis; 2(8):763-768 1981

Cells from human bladder epithelium cell lines HU1689, HU1752, and HU1765 and primary bladder epithelial cells from Wistar rats were exposed in vitro for 24 hr to radioactively-labeled carcinogens dissolved in the medium: [1,3,6-3H]benzo[a]pyrene (BP) 1.5 uM; [G3H]aflatoxin B1 (AFB) 1.5 uM; [14C]N-nitrosodimethylamine (DMNA) 100 uM; [ethyl-1-14C]N-nitrosoethylmethylamine (EMNA) 100 uM; and [2,5-14C]N-nitrosopyrrolidine (NPy) 100 uM. The metabolism of the carcinogens was assayed by the release of metabolites into the culture medium and the binding of radioactive metabolites to DNA. The human bladder cells retained 2 the capacity to metabolize chemical carcinogens. Binding of DNA occurred to a similar extent in all three cell lines. More BP was bound to DNA in human bladder cells than in rat bladder cells. More than 90% of the metabolites of BP in human cells consisted of organo-soluble products, primarily the 9,10-and 7,8-BP diols. N-nitrosamine metabolism produced CO2. NPy was oxidized in both the alpha and beta positions, predominantly alpha in human cells. EMNA was apparently metabolized, but did not bind to DNA. The results suggest that the human bladder may be able to activate carcinogens that come into direct contact with the epithelium, and that it utilizes pathways that are different from those found in other tissues and cells. (38 Refs)

15. URINARY GLYCOSAMINOGLYCAN EXCRETION AS A BIOCHEMICAL MARKER IN PATIENTS WITH BLADDER CARCINOMA.

Hennessey PT, Hurst RE, Hemstreet GP, Cutter G
(c/o Hurst) 102 BMS Building, Univ. Alabama Birmingham, Birmingham, AL, 35294
Cancer Res; 41(10):3868-3873 1981

Urinary glycosaminoglycan excretion was examined in 25 individuals with bladder cancer in comparison to glycosaminoglycan excretion by 8 normal individuals. Urinary glycosaminoglycan was isolated by gel filtration and quantified as macromolecular uronate concentration. Electrophoresis in calcium acetate and densitometry of Alcian blue-stained electrophoretograms were used to separate and quantify the relative amounts of individual glycosaminoglycans. Elevated excretion of macromolecular uronate was noted in 53% of the cancer cases. The highest levels were found among individuals with metastatic disease. Three electrophoretic bands were always detected in the control and cancer groups: chondroitin sulfate, heparin sulfate (both confirmed by chemical and enzymatic degradation), and a third band (Band 1) of unknown composition. A fourth band, corresponding to dermatan sulfate, was seen in some high-grade metastatic tumors. Band 1 excretion was elevated in a significant fraction of all patients. Seven of 12 metastastic cases but only 2 of 13 localized cases showed increased heparin sulfate excretion. Diagnostic limits were drawn from the observed distributions of normals, and with these limits 92% of the cancer cases, including 12 of 12 metastatic cases, could be identified. The results strongly suggest noninvasive urinary glycosaminoglycan analysis may well provide a new biochemical approach for detecting and monitoring the pathogenesis of bladder cancer. (Author abstract) (21 Refs)

16. DETECTION OF MAMMALIAN CELL MUTAGENS IN URINE FROM CARCINOGEN-DOSED MICE.

Amacher DE, Turner GN, Ellis JH
Drug Safety Evaluation Dept., Pfizer Central Res., Groton, CT, 06340
Mutat Res; 90(1):79-90 1981

Urine was collected from male CD-1 mice dosed by oral gavage with either 300 mg/kg 2-aminofluorene (AF), 150 mg/kg cyclophosphamide (CY), or 200 mg/kg lucanthone (LU), and added directly to L5178Y TK+/- mouse lymphoma cultures (heterozygous at the thymidine kinase locus for the induction of trifluorothymidine-resistant (TFT-R) mutants). After 3 hr incubation, urine from the three different groups of rats produced significant, dose-dependent increases in frequency of TFT-R mutants. When the drugs were tested directly as mutagens in L5178Y TK+/- cells, LU and CY were positive both with and without metabolic activation, but AF required activation. Significant differences in the direct response of Salmonella typhimurium and L5178Y cells to these compounds indicate that the two cell types may not detect the same chemical entities as proximate mutagens. Urinary metabolites of AF, CY, and either the parental molecule or metabolites of LU can readily be detected as mutagens in a mammalian cell assay. (28 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

17. CYST FORMATION IN RAT KIDNEY INDUCED BY CIS-PLATINUM ADMINISTRATION.

Dobyan DC, Hill D, Lewis T, Bulger RE
Dept. Pathology and Lab. Medicine, Univ. Texas Health Science Center, Post Office Box 20708, Houston, TX, 77025
Lab Invest; 45(3):260-267 1981

The long-term pathologic effects of the antitumor drug cis-diamminedichloroplatinum II (CP) on the structure of the rat kidney were investigated. Light microscopy and transmission and scanning electron microscopy were used to characterize the morphologic changes 2 wk, 4 wk, and 6 mo after ip injection of CP to rats. At all time intervals examined, the S3 segment of the proximal tubule located in the outer stripe of the medulla showed the most consistent pattern of injury. Two wk after CP, the proximal tubules located in the outer stripe region as well as the medullary rays were widely dilated and lined by low-lying epithelial cells, many of which contained large atypical nuclei. Many tubules still showed evidence of necrosis, whereas other tubules appeared to be undergoing atrophic changes. After 4 wk, proximal tubular dilation continued resulting in the formation of numerous microcysts in the region of the outer stripe. These changes appeared to progress, and after 6 mo large cysts (mean diameter 2,152 +-1,241 um) were identified which involved the entire outer stripe, with many of these cysts extending to the subcapsular cortex. The kidneys at this time period showed a pattern of chronic renal injury in the outer stripe, and this damage was now also observed in the cortex. In several animals, small foci of abnormal foam cells surrounded by a basal lamina could be identified. We conclude that CP has a pronounced long-term effect and causes cyst formation in the rat kidney. (Author abstract) (22 Refs)

18. SARCOMATOUS VARIANT OF WILMS' TUMOR. A LIGHT AND IMMUNOHISTOCHEMICAL STUDY OF FOUR CASES.

Giangaspero F, Zanetti G, Mancini A, Rosito P
Istituo di Anatomia ed Istologia Patologica, Policlinico S. Orsola, Via Massarenti 9, 40138 Bologna, Italia
Tumori; 67(4):367-373 1981

Four cases of infantile sarcomatous renal tumors are reported. Rhabdomyoblastic differentiation was investigated in these tumors by the immunoperoxidase method using antimyoglobin sera. Rhabdomyoblastic cells were found in two cases in a metastasis of one case in which the primary tumor was composed by undifferentiated cells negative for myoglobin stain. The histogenesis of these neoplasias is discussed, and it is suggested that they are a sarcomatous variant of Wilms' tumor. (Author abstract) (21 Refs)

19. HISTOCHEMICAL INVESTIGATIONS ON HUMAN BLADDER.

Aeikens B
Medizinische Hochschule Hannover, Urologische Klinik, Karl-Wiechert-Allee 9, Postfach 180, D-3000 Hannover-Kleefeld, W. Germany
Urol Int; 36(3):152-157 1981

The histochemical enzyme activity of alkaline phosphatase, nonspecific esterase, 5-nucleotidase, beta-glucuronidase, glucose-6-phosphatase, succinate dehydrogenase, and glucose-6-phosphate dehydrogenase in human bladder cancer was investigated. Tumors of 84 patients, classified into grades I-III according to the WHO classification, were compared with 12 normal and 16 inflamed bladder epithelia. As a rule, loss of alkaline phosphatase activity and a decrease of nonspecific esterase activity was found in most of these tumors. The activity of beta-glucuronidase was decreased and compared with normal tissue, also the activity of 5-nucleotidase. The succinate dehydrogenase activity in tumor tissue was frequently increased, whereas glucose-6-phosphate dehydrogenase did not show any significant reaction. (Author abstract) (22 Refs) (In GER)

20. ULTRASTRUCTURE OF MAJOR CELLULAR TYPES OF HUMAN TRANSITIONAL CELL CARCINOMAS OF THE URINARY BLADDER.

Galyrov AG
Lab. Histochemistry and Electron Microscopy, All-Union Cancer Res. Center, Moscow, USSR
Arkh Patol; 43(6):46-52 1981

The results of electron microscope examination of 33 specimens of human transitional cell carcinoma of the urinary bladder are reported. Transitional cell carcinomas contained two groups of tumor cells. The group of differentiated tumor cells consisted of superficial, intermediate, and squamous epithelial cells, while the group of poorly differentiated cells consisted of basal epithelial cells. Of 33 specimens of transitional cell carcinoma, 32 contained superficial cells, 29 contained intermediate cells, 33 contained basal cells, and 5 contained squamous cells; combination of all cell types was recorded in 4 tumors. (16 Refs) (In RUS)

21. AN IN VITRO CLONAL ASSAY FOR BLADDER CANCER: STUDIES OF THE BIOLOGIC POTENTIAL OF THE UROTHELIUM AND DETERMINATION OF IN VITRO SENSITIVITY TO CYTOTOXIC AGENTS.

Stanisic TH, Buick RN, Trent JM, Fry SE, Salmon SE
Dept. Surgery/Urology, Univ. Arizona, Health Sciences Center, Tucson, AZ, 85724
J Surg Oncol; 18(1):67-72 1981

We have applied an in vitro colony-forming assay system to the study of primary urothelial explants obtained transurethrally by bladder barbotage and tumor biopsy from 91 patients. Urothelial cells obtained by bladder barbotage from patients with bladder cancer and from a 'control' group of individuals exhibit differential capacity to clone in agar. Of samples from bladder cancer patients, 88% formed colonies, whereas only 27% of these from a 'control' group did so. Of samples from a 'suspicious' patient group, 70% formed colonies. In vitro drug sensitivity studies of cells obtained by biopsy of solid tumors demonstrate a spectrum of drug sensitivity to cytotoxic agents. (Author abstract) (5 Refs)

22. F-ACTIN AGGREGATES IN TRANSFORMED CELLS.

Carley WW, Barak LS, Webb WW
Sch. Applied Physics and Engineering, Cornell Univ., Ithaca, NY, 14853
J Cell Biol; 90(3):797-802 1981

Polymerized actin has been found aggregated into distinctive patches inside transformed cells in culture. The F-actin-specific fluorescent probe, nitrobenzoxadiazole-phallacidin, labels these F-actin aggregates near the ventral cell surface of cells transformed by RNA or DNA tumor viruses, or by chemical muta-

gens, or spontaneously. Their appearance in all eight transformed cell types studied suggests their ubiquity and involvement in transformation morphology. Actin patches developed in normal rat kidney (NRK) cells transformed by a temperature-sensitive mutant of Rous sarcoma virus (LA23-NRK) within 30 min after a shift from the nonpermissive (39 C) to the permissive temperature (32 C). Patch appearance paralleling viral src gene expression tends to implicate pp60src kinase activity in destabilizing the cytoskeleton. However, appearance of the actin aggregates in cells not transformed by retrovirus calls for alternative mechanisms, perhaps involving an endogenous kinase, for this apparently common trait. (Author abstract) (26 Refs)

23. URINE FROM PATIENTS WITH TRANSITIONAL-CELL CARCINOMA STIMULATES MIGRATION OF CAPILLARY ENDOTHELIAL CELLS.

Chodak GW, Scheiner CJ, Zetter BR
300 Longwood Ave., Boston, MA, 02115
N Engl J Med; 305(15):869-874 1981

Capillary-endothelial-cell-migration (CECM) activity was assayed in 125 urine samples from 104 subjects (82 with malignant and nonmalignant diseases and 22 with no acute disease). For each sample, the percentage of increase in cell migration was calculated by comparing the mean area of the tracks made by cells incubated in culture medium containing test urine with that of tracks made by cells incubated in medium alone. Dialyzed, concentrated urine from patients with transitional-cell carcinoma (TCC) of the bladder stimulated CECM in vitro (42% increase). Activity was consistently higher in patients with tumors and was consistently decreased to control levels 3-6 days after tumor removal by transurethral resection or cystectomy. New tumor growth was revealed by increased levels of activity 80-250 days after tumor removal. In patients with no tumor recurrence, levels of activity remained low. One of two patients with a history of TCC who exhibited increased activity had a positive urinary cytologic test 90 days later; biopsy of the bladder revealed premalignant changes. Low levels of activity were found in urine from normal controls, from patients with non-neoplastic urologic disease, and from patients with prostate tumors. (12 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

24. CELL SURFACE ANTIGENS OF HUMAN RENAL CANCER DEFINED BY MOUSE MONOCLONAL ANTIBODIES: IDENTIFICATION OF TISSUE-SPECIFIC KIDNEY GLYCOPROTEINS.

Ueda R, Ogata S-I, Morrissey DM, Finstad CL, Szkudlarek J, Whitmore WF, Oettgen HF, Lloyd KO, Old LJ
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Proc Natl Acad Sci USA; 78(8):5122-5126 1981

Seventeen monoclonal antibodies derived from fusions with spleen cells of mice immunized with established culture lines of renal cancers identified 9 cell-surface antigenic systems. Six of the systems (gp160, S25, gp120r, gp120nr, gp115, and V1) represent antigens not previously described. the other three systems are related to HLA-A, -B, and -C heavy chain and A and B blood group antigens. The most restricted of the newly described antigens are gp160, S25, and gp120r. These determinants are found only on cells of renal origin, both normal and malignant, and represent differentiation antigens of human kidney. In addition to the difference in the mol wt of two of these antigens, gp160, S25, and gp120r can be distinguished on the basis of differential expression on a panel of cultured renal cancers and normal kidne y epithelium and fetal kidney cells. Glycoproteins bearing gp120r share a determinant with renal gp120nr (as indicated by sequential precipitations with monoclonal antibodies that detect gp120r and gp120nr), but gp120nr is found on a broader range of cell types, including fibroblasts and cell lines derived from lung, bladder, and colon cancers. The two other new systems, gp115 and V1, have characteristics of broadly occurring differentiation antigens but can be distinguished from each other and from gp120nr by differences in mol wt, heat stability (V1 is a heat-stable determinant), and differential expression on cell types of diverse origin. (Author abstract) (9 Refs)

25. LYMPHOCYTE CYTOTOXICITY AGAINST AUTOLOGOUS BLADDER TUMOR CELLS IN HUMANS, INVESTIGATED BY USE OF A CHROMIUM-51 RELEASE ASSAY.

Jacobsen F
Univ. Inst. Pathology, Aarhus Amtssygehus, DK-8000 Aarhus C, Denmark
Acta Pathol Microbiol Scand [C]; 89(3):175-180 1981

A technique for isolation of a single cell suspension of viable tumor cells from bladder tumor biopsies is described. By application of the tumor cells as targets in a 51chromium release assay, the cytotoxicity of autologous lymphocytes was measured in 38 patients with transitional-cell tumors of the urinary bladder. The lymphocyte-mediated cytotoxicity was evaluated in relation to the histological grade and clinical stage of the bladder tumors. No significant correlations were found between the autologous cytotoxicity and the grade or stage of the bladder tumors. (Author abstract) (23 Refs)

26. THE DETECTION OF TRANSITIONAL CELL BLADDER CANCER ANTIGEN ON ESTABLISHED CELL LINES.

Boxer RJ, Sofen H, Saxon A
(c/o Saxon) Dept. Medicine, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
Invest Urol; 19(2):70-74 1981

An antigen with mol wt of 72,000 daltons has been detected on established cell culture lines of transitional cell carcinoma. Using heterologous (rabbit) antisera and absorptions with malignant and nonmalignant cells, fetal tissues, and tissue culture proteins, we have shown that the antigen has specificity for in vitro transitional cell carcinoma. (Author abstract) (36 Refs)

REVIEWS AND OTHER RELATED STUDIES

27. CHROMOSOME ABNORMALITIES, TUMOURS AND DEVELOPMENTAL DISORDERS.

Gropp A
Institut Pathologie Med Hochschule Lubeck, Ratzeburger Allee 160, D-2400 Lubeck, W. Germany
Klin Wochenschr; 59(17):965-975 1981

Clonal chromosome disorders occurring or acquired at any postnatal age are often closely related to the origin of tumors. In man the Ph1-chromosome (9; 22) anomaly in CML or the 8; 14 translocation in the African malignant Burkitt Non-Hodgkin lymphoma are, among other cases, prominent examples. On the other hand, constitutive, inherited or novel chromosome anomalies conveyed from the zygote t o all tissues of the organism may cause a higher risk for the origin of tumors. Rarely, inheritable minor structural chromosome mutations are known to determine the occurrence of dysontogenic tumors, as eg, nephroblastoma, but it is assumed that more such cases will become elucidated in the future. As a special phenomenon, true hydatiform mole is a tumor of the placental tissue due to a disorder of intragenome regulation. Constitutive or numerical structural chromosome anomalies of man are a frequent cause of early or late abortion or of abnormal development and malformation. Despite the predominating principle of selective fetal elimination, a few anomalies such as Down's syndrome, may escape to longer survival due to the relatively mild effects of chromosome 21 triplication. Trisomies which represent in man the most frequent type of chromosome disorders, can be induced, and systematically studied in an experimental model of the mouse. This allows the elaboration of the developmental profiles of all trisomies (and monosomies) of the mouse. Also, the above mentioned principle of selective elimination of abnormal implants can be analyzed experimentally. Although the developmental span of a trisomic zygote is limited, there is evidence that cells and tissues isolated from the chromosomally abnormal organism can survive much longer. Thus, hemopoietic stem cells, at least in Ts 12 and 19 of the mouse, can be rescued from trisomic fetuses by transferring them to lethally irradiated adult mice, whose blood forming organs may eventually become permanently repopulated by the trisomic cell lineage. This type of experiments is suited for closer analyses of potential function vs defects of chromosomally abnormal cellular systems, eg, with regard to growth and development. (Author abstract) (55 Refs) (In GER)

28. EARLY DETECTION OF OCCUPATIONAL HAZARDS.

McDonald JC, Harrington JM

TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, London WC1E 7HT, England

J Soc Occup Med; 31(3):93-98 1981

Because of the rate of technological change, the time interval between exposure to a hazard and the appearance of its effects may be very long. Surveillance procedures for occupationally related diseases and injuries in Britain are generally regarded as inadequate. Reported intervals between the first suspicion and general acceptance of some occupational hazards have varied from 2 to 59 yr (for angiosarcoma due to vinyl chloride monomer and bladder cancer due to aromatic amines, respectively). Some occupational diseases have only been recognized by chance, having been completely missed by existing methods of reporting or the discovery was not reported. Detection of occupational hazards has frequently depended upon astute clinical observation; a system of rapid informal communication about such 'hunches' is ne eded. There are parallels for this idea in the history of determining the etiology of numerous communicable diseases. The essentially informal reporting networks for communicable diseases operating in Britain and the United States are linked to central analysis units which can initiate rapid field studies when indicated. The establishment of an analogous system for occupational disease is advocated. (no Refs)

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CHEMICAL CARCINOGENESIS

1. TOXICOLOGICAL ASPECTS OF POLYCYCLIC AROMATIC HYDROCARBONS (PAH).
De Fernicola NA, De Azevedo FA
Divisao de Toxicologia e Ecotoxicologia, Diretoria de Tecnologia e Desenvolvimento, Sao Paulo, Brazil
Rev Bras Saude Ocup; 33(9):62-68 1981
In POR

2. EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS: SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.
International Agency for Research on Cancer
International Agency for Res. on Cancer, Lyon, France
IARC Monogr Eval Carcinog Risk Chem Hum; 26:1-411 1981

3. STUDIES ON THE ROLE OF ORAL CONTRACEPTIVE USE IN THE ETIOLOGY OF BENIGN AND MALIGNANT LIVER TUMORS.
Mettlin C, Natarajan N
Cancer Control and Epidemiology, Rosewell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Surg Oncol; 18(1):73-85 1981

RADIATION CARCINOGENESIS

4. EXPERIMENTAL RADIATION CARCINOGENESIS: WHAT HAVE WE LEARNED?
Fry RJ
Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Radiat Res; 87(2):224-239 1981

5. INFLUENCE OF NONCARCINOGENIC SECONDARY FACTORS ON RADIATION CARCINOGENESIS.
Little JB
Lab. Radiobiology, Harvard Univ., Sch. Public Health, Boston, MA, 02115
Radiat Res; 87(2):240-250 1981

6. MEDICAL IRRADIATION IN JAPAN - STOCHASTIC RISK ESTIMATION AND ITS REDUCTION.
Hashizume T
Div. Physics, National Inst. Radiological Sciences, 9-1 Anagawa 4-Chome, Chiba Shi 260, Japan
Nippon Igaku Hoshasen Gakkai Zasshi; 41(5):445-474 1981
In JPN

7. RADIOACTIVITY IN DRINKING WATER.
Cothern CR
Office of Drinking Water, Environmental Protection Agency, Washington, DC
Radioactivity in Drinking Water. Available from National Technical Information Service, Springfield, VA, as PB81-192833:, 79 pp., 1981.

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

8. EPIDEMIOLOGY OF GASTROINTESTINAL CANCER.
Miller AB
NCIC Epidemiology Unit, Univ. Toronto, McMurrich Building, Toronto, Ontario M5S 1A8, Canada
Compr Ther; 7(8):53-58 1981

9. EPIDEMIOLOGICAL ASPECTS OF ESOPHAGEAL CANCER.
Ruggieri M, Tosato F, De Rocco K, Lepore M, Cipriano E, Paolini A
IV Cattedra di Clinica Chirurgica Generale e Terapia Chirurgica, Universita degli Studi di Roma, Rome, Italy
Recenti Prog Med; 70(5):545-556 1981
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10. PANCREATIC CANCER.
Cohn I, Hastings PR
Dept. Surgery, Louisiana State Univ., 1542 Tulane Ave., New Orleans, LA, 70112
UICC Tech Rep Ser. Vol. 57, Issue 12, 142 pp., 1981.

11. GENETICALLY DETERMINED SUSCEPTIBILITY TO CANCER.
Marks PA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Blood; 58(3):415-419 1981

12. ETIOLOGY, ROLE AND DETECTION OF CHROMOSOMAL ABERRATIONS IN MAN.
Fabricant JD, Legator MS
Dept. Preventive Medicine, Div. Environmental Toxicology, Univ. Texas Medical Branch, Galveston, TX, 77550
JOM; 23(9):617-625 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

13. INDUSTRIAL CARCINOGENESIS.
Vickers CF
Dept. Dermatology, Univ. Liverpool, Liverpool L69 3BX, England
Br J Dermatol; 105(Suppl21):57-61 1981

14. ENVIRONMENT AND HEALTH (LITERATURE REVIEW).
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Zh Eksp Klin Med; 21(3):287-292 1981
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15. LIFESTYLE AND CANCER.
Higginson J
International Agency for Res. on Cancer, Lyon, France
Cancer Forum; 5(1):4-14 1981

16. ASBESTOS, AN ENVIRONMENTAL POLLUTANT.
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Institutul de igiena si sanatate publica, Iasi, Romania
Igiena; 30(1):1-9 1981
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17. REVIEW OF UICC PROGRAM ON SMOKING AND LUNG CANCER.
Gray N
Smoking and Cancer Program, UICC, 3 rue du Conseil General, 1205 Geneva, Switzerland
Cancer Forum; 5(1):15-18 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

18. EXPERIMENTAL APPROACHES TOWARDS THE BIOCHEMICAL ANALYSIS OF CHEMICAL CARCINOGENESIS.
Laishes BA
McArdle Lab. for Cancer Res., Univ. Wisconsin Medical Sch., Madison, WI, 53706
ACS Symp Ser; 160:197-215 1981

19. FIBRONECTIN AND RELATED TRANSFORMATION-SENSITIVE CELL SURFACE PROTEINS (ONCOLOGY OVERVIEW).
International Cancer Research Data Bank
ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Fibronectin and Related Transformation-Sensitive Cell Surface Proteins (Oncology Overview) Chen, L B, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923001:, OB-81/01:95pp. 1981

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Preneoplastic Lesions of the Mammary Gland (Oncology Overview) Medina, D, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923002; OB-81/02:134pp. 1981

21. LYMPHOCYTE DIFFERENTIATION: AN ESSENTIAL BASIS FOR THE COMPREHENSION OF LYMPHOID NEOPLASIA.
Magrath IT
Pediatric Oncology Branch, Div. Cancer Treatment, NCI, NIH, Public Health Service, United States Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(3):501-514 1981

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22. FACTORS STIMULATING AND INHIBITING TUMOR GROWTH IN CARCINOGENESIS.
Kochergina NI, Kosova IP
Res. Lab. Experimental Immunobiology, Moscow, USSR
Usp Sovrem Biol; 91(3):403-418 1981
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Berenblum I, Armuth V
Weizmann Inst. Science, Rehovot, Israel
Biochim Biophys Acta; 651(1):51-63 1981

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24. BURKITT'S LYMPHOMA.
Ziegler JL
NCI, Bethesda, MD, 20205
N Engl J Med; 305(13):735-745 1981

25. REVIEW ARTICLE. REGULATION OF EXPRESSION OF THE INTEGRATED RETROVIRUS GENOME.
Weinberg RA, Steffen DL
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
J Gen Virol; 54(part1):1-8 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

26. THE DEVELOPMENT AND VALIDATION OF MUTAGENICITY SCREENING TESTS.
Durkin PR, Santodonato J
Center for Chemical Hazard Assessment, Syracuse Res. Corporation, Merill Lane, Syracuse, NY, 13210
Tappi; 64(9):153-159 1981

27. SHORT-TERM TEST SYSTEMS FOR POTENTIAL MUTAGENS AND CARCINOGENS: I. MICROBIAL TESTS (ONCOLOGY OVERVIEW).
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Short-Term Test Systems for Potential Mutagens and Carcinogens: I Microbial Tests (Oncology Overview) Simmon, V F; Peirce, V; eds This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-922903:; OK-81/03:124pp. 1981

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Eveson JW
Dept. Oral Medicine and Pathology, Guy's Hosp., London SE1 9RT, England
J Oral Pathol; 10(3):129-146 1981

29. THE CHROMOSOMES IN HEMATOLOGY.
Berger R
Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies et les Maladies du Sang, UER d'Hematologie, Hopital Sant-Louis, 2 place du Dr. Fournier, 75475 Paris Cedex 10, France
Cancer Genet Cytogenet; 4(1):69-88 1981

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MARCH, 1982

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. ATLAS OF CANCER MORTALITY IN THE PEOPLE'S REPUBLIC OF CHINA. AN AID FOR CANCER CONTROL AND RESEARCH.

Li JY, Liu BQ, Li GY, Chen ZJ, Sun XD, Rong SD
Dept. Cancer Epidemiology, Cancer Inst. Chinese Acad. Medical Sciences, 2, Yabao Lu, Chaoyang, Qu, Beijing, People's Republic of China
Int J Epidemiol; 10(2):127-133 1981

A set of maps which display the patterns of cancer mortality in China has been p repared and published by the China Map Press. The 200 page atlas was edited by the National Cancer Control Office of the Ministry of Health and the Nanjing Institute of Geography of the Chinese Academy of Sciences on the basis of a nation-wide cancer mortality survey. The Cancer Institute of the Chinese Academy of Medical Sciences with related Colleges, Universities and Institutes provided the data and took part in the preparation of the atlas, which is published both in Chinese and English. Fifty eight maps and several dozen charts depict, in seven colors, the mortality distribution in the 2,392 counties and county-level administrative units of nine types of cancer common in China - stomach, esophagus, liver, cervix, lung, colon and rectum, breast. nasopharynx, and leukemia as well as five less common cancers - brain tumors, malignant lymphoma, cancer of the bladder, of the penis, and choriocarcinoma. The Atlas of Cancer Mortality will be an important new aid for cancer control and research in the People's Republic of China. (Author abstract) (10 Refs)

2. CANCER OF THE MALE BREAST. A REVIEW OF 17 CASES.

Kuo SJ, Wang CC, Liu TC, Wu SJ, Peng FK, Lee C
Dept. Surgery, Veterans General Hosp., Taipei, Taiwan
J Formosan Med Assoc; 80(5):523-529 1981

Review of hospital records from 1961-1979 uncovered 17 cases of breast cancer in males, all of whom presented with palpable lumps. Histologically 14 were carcinoma (13 adenocarcinoma, 1 epidermoid carcinoma) and 3 sarcoma (fibrosarcoma, leiomyosarcoma and malignant schwannoma). Karyotypic analyses of six patients chosen at random revealed normal chromosome number but all had abnormal marker chromosomes in the B/D Group and ring chromosomes in the F Group. Subsequent cancers were found in lung (1 case) and gastric and urinary bladder (1 case). Radical mastectomy was used in nine patients; in six with axillary metastases, five received postoperative radiotherapy, one chemotherapy. Four of these five died 2-6 yr after therapy, two of other cancers; one patient was lost to follow-up. Of 11 without axillary involvement, 9 are alive 0.5-10 yr after operation; 2 were lost to follow-up. Six patients survived 5 yr or more. (8 Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

3. MORTALITY AMONG RUBBER WORKERS. III. CAUSE-SPECIFIC MORTALITY, 1940-1978.

Delzell E, Monson RR
Dept. Epidemiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115
JOM; 23(10):677-684 1981

This report describes mortality occurring between 1940 and mid-1978 among 29,087 men and women employed in a rubber plant for at least 2 yr. Mortality patterns for the period July 1, 1974, to July 1, 1978, were compared to previously published findings for January 1, 1940, through June 30, 1974. Expected numbers of deaths were based on U.S. general population mortality data. There were excess d eaths from bladder cancer and leukemia among white male union members during both follow-up periods. During recent follow-up of white male union members employed for at least 5 yr, there were excesses in deaths from three additional cancers: esophageal cancer (11 observed/4.8 expected), biliary and liver cancer (6 observed/ 3.3 expected) and lymphoma and multiple myeloma (14 observed/5.8 expected). Evidence from other studies of rubber workers suggests that observed excesses in deaths from bladder cancer and leukemia are related to workplace exposures. The present findings suggest that occupational exposures etiologically relevant to these diseases may not have been reduced in recent yr or that sufficient time has not elapsed for such reductions to result in decreased mortality. Further investigation is required to clarify the contribution of occupational factors to observed excesses in deaths from cancers of the esophagus and the biliary passages and liver and from lymphoma and multiple myeloma. (Author abstract) (26 Refs)

4. A STUDY OF THE GEOGRAPHICAL PATTERN OF CANCER MORTALITY FOR SELECTED SITES BY MEANS OF FACTOR ANALYSIS.

Inaba Y, Yanai H, Takagi H, Yamamoto SI
Dept. Hygiene, Juntendo Univ., Japan
Soc Sci Med [Med Geogr]; 15(1):233-244 1981

Factor analysis of the geographical distribution of cancer mortality in 46 Japanese prefectures during 1958-1971 revealed a significant correlation between the rate of primary industry and skin, prostate, lymphoid tissue, or bladder cancer and leukemia in men. In women, uterine and liver cancer and leukemia correlated positively with natural environmental factors (temperature, precipitation). Lung, intestinal, and oral cancer correlated with population density and appeared to be related to industrialization or urbanization. There was also a significant positive correlation between the rate of primary industry and pancreas and bile duct cancer in women. Esophageal cancer did not correlate with the primary industry rate, the natural environmental factors, or population density. Food consumption in Japan and 24 other countries also was analyzed. Despite the different data sources, similar clustering of cancer sites was noted; ie, prostate, skin, and leukemia for men, skin and leukemia for women, and intestines and lungs for both sexes. (15 Refs)

5. RADIATION LOAD DURING COMPUTER TOMOGRAPHY.

Stargardt A, Potzschke B
Institut fur Rontgendiagnostik, Bereich Medizin der Humboldt-Universitat, Schumannstr. 20/21, DDR-1040 Berlin, E. Germany
Radiol Diagn (Berl); 22(3):305-308 1981

The gonadal and somatic radiation doses and risks of computer tomography were calculated for examinations of the abdomen, thorax, and skull. The radiation dose to the ovaries and testicles was found to be highest during examinations of the urinary bladder and reproductive organs, and lowest d uring computer tomography of the skull. The risk of cancer or leukemia (per 1,000,000 examinations at a surface dose of 1.4 rads per layer) is highest (38) in the computer tomographic diagnosis of lymphoma, lower during the examination of the abdomen (32), during search for primary tumors (36), and during examination of the urinary bladder region and reproductive organs (28), and lowest during cranial tomography (10). (no Refs) (In GER)

6. TATTLETALE LESIONS: A WARNING IN DISGUISE.

Rosen T, Mills JM
Dept. Dermatology, Univ. Texas Medical Sch., Houston, TX
RN; 44(10):44-45 1981

Suggestions are given for recognition of superficial skin lesions which may represent Bowen's disease. The disease results in development of additional premalignant and malignant skin tumors, including cancer of the skin and sweat glands and malignant melanoma in almost half of patients. Such patients are also at increased risk for development of internal cancer, usually of the respiratory, gastrointestinal, or urogenital systems. (4 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

7. COMPARISON OF THE CARCINOGENICITY OF METHYLAZOXYMETHANOL-BETA-D-GLUCOSIDURONIC ACID IN CONVENTIONAL AND GERMFREE SPRAGUE-DAWLEY RATS.

Laqueur GL, Matsumoto H, Yamamoto RS
(c/o Matsumoto) Dept. Agricultural Biochemistry, Univ. Hawaii, 1800 East-West Rd., Honolulu, HI, 96822
JNCI; 67(5):1053-1055 1981

Methylazoxymethanol-beta-D-glucosiduronic acid (MAM-GlcUA) was administered to young adult male Sprague-Dawley rats by oral and ip routes. Most neoplasms developed in rats that had received the compound po. The most prevalent site for the neoplasms was the intestinal tract, predominantly the colon. Comparatively fewer tumors occurred in the liver and kidneys. Germfree rats did not develop tumors when MAM-GlcUA was administered either po or ip. (Author abstract) (9 Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

8. BLADDER CARCINOGENESIS IN MICE INDUCED BY N-BUTYL-N-(4-HYDROXYBUTYL)NITROSAMINE AND N-ETHYL-N-(4-HYDROXYBUTYL)NITROSAMINE WITH REFERENCE TO THE EFFECT OF CYCLOPHOSPHAMIDE.

Numoto S, Yoshida M, Otsuka H
Second Dept. Pathology, Sch. Medicine, Tokushima Univ., Kuramoto-cho 3-18-15, Tokushima 770, Japan
Gan; 72(5):647-654 1981

The carcinogenicities of N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) and N-ethyl-N-(4-hydroxybutyl)nitrosamine (EHBN) on the urinary bladder were compared in male BALB/c mice. The effect of cyclophosphamide (CPA) on the carcinogenicities was also investigated. The carcinogenic activity on the bladder mucosa of EHBN was similar to that of BBN, and there was no difference in the growth patterns, histological types or invasive characters of carcinoma induced by BBN and EHBN. Benign or malignant tumors of vascular origin developed in the urinary bladders of 15 mice treated with these carcinogens. The incidence of vascular tumors induced by EHBN was significantly higher than that of tumors induced by BBN. Ip injections of CPA seemed to have no effect in the incidence of bladder carcinomas induced by these carcinogens, or on the development of vascular tumors in the bladder wall induced by EHBN. (Author abstract) (18 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

9. SPECIES DIFFERENCES IN MUTAGENICITY, COVALENT PROTEIN BINDING AND NEPHROTOXICITY OF THE FLAME RETARDANT TRIS(2,3-DIBROMOPROPYL) PHOSPHATE (MEETING ABSTRACT).

Soderlund E, Dybing E, Nelson SD
Department of Toxicology, National Institute of Public Health, Olso, Norway
Acta Pharmacol Toxicol; 49(Suppl1):48 1981

Tris(2,3-dibromopropyl)phosphate (Tris-BP), the major flame retardant formerly used in US sleepwear, is a potent mutagen, a nephrocarcinogen and an acute nephrotoxin. Hepatic microsomes from rats, mice, hamsters, and guinea pigs are all able to activate Tris-BP to mutagenic products in the Salmonella microsome quantitative reversion assay, mice microsomes being the most and guinea pig microsomes the least active. Phenobarbital (PB)-pretreatment increases the mutagenic activity with all microsomal preparations, whereas 3-methylcholanthrene (MC)-pretreatment decreases Tris-BP mutagenicity in rats and mice and gives a moderate increase in hamsters and guinea pigs. Hepatic microsomes from all species tested have approx similar basal capabilities in converting Tris-BP to covalently protein bound products in vitro; PB-pretreatment increases binding rates in all preparations, MC-pretreatment increases Tris-BP covalent binding with hamster and guinea pig microsomes but not with microsomes from rat or mouse liver. Tris-BP binds covalently to liver protein in vivo in all species

and to kidney protein in hamster, guinea pig and mouse to the same degree. In rat kidneys, on the other hand, seven fold higher protein binding levels are found compared to liver, correlating with the finding that kidney is the target organ in this species. None of the other species showed any Tris-BP-induced kidney damage. (no Refs)

10. (NA+ + K+)-STIMULATED ATPASE OF HUMAN KIDNEY, NORMAL AND ADENOCARCINOMA. PHOSPHORYLATION AND INHIBITION BY ANTITUMOR PROTEINS.

Zaheer A, Singh D, Montgomery R
Dept. Biochemistry, Univ. Iowa, Iowa City, IA, 52242
Biochem Biophys Res Commun; 102(1):86-92 1981

To evaluate the effect of antitumor proteins on metabolism of cultured tumor cells, (Na+ + K+)-stimulated ATPase isolated from normal human kidney and from renal clear cell adenocarcinoma was treated with macromomycin (MM), auromomycin (AM), largomycin (LM), and NSC 327459. MM, LM, and NSC 327459 (all 50 ug/ml) caused 73.4-93.4% inhibition of enzyme purified from adenocarcinoma. LM and NSC 327459 produced 16.5-23.2% inhibition of the enzyme from normal kidney, but MM and AM did not affect normal kidney ATPase. AM was also ineffective against the enzyme from kidney adenocarcinoma. Cyclic AMP (5 uM) caused a 6x stimulation of the rate of phosphorylation of normal enzyme, compared with a 3x increase of phosphorylation rate for the tumor enzyme. Phosphorylation reduced the enzyme activities: the normal ATPase exhibited 28.8% of original activity and the tumor enzyme showed only 19.1%. The normal enzyme was now sensitive to MM inhibition (approx 40% at 10 ug/m). (16 Refs)

11. ACTIVATION OF N-2-ACETYLAMINOFLUORENE BY TARGET AND NONTARGET SYRIAN GOLDEN HAMSTER CELLS (MEETING ABSTRACT).

Polley JA, Raineri R, Ernst MK, Andrews AW, Pienta RJ
Frederick Cancer Research Center, Frederick, MD, 21701
In Vitro; 17(3):222 1981

The ability to metabolize and activate N-2 acetylaminofluorene (AAF) of Syrian golden hamster kidney, bladder, small intestine, lung and liver cells was compared with that of hamster embryo fibroblasts. At varying times after isolation, cells were exposed to 5 ug [14C]-AAF for 3, 6 or 24 hr. The level of AAF remaining and the amount bound to cellular components were determined. Within 3 hr, hepatocytes and intestinal cells had metabolized 95% of the AAF. Within 6 hr lung cells had metabolized 50%, and kidney cells 20%. By contrast, fibroblasts and bladder cells had metabolized only 20-25% in 24 hr. The amount of material bound to cellular components was proportional to the amount of AAF metabolized. A second measure of activation was the ability of intact organ cells to metabolize AAF to a form mutagenic in Salmonella TA 1538. Revertant numbers were much increased above background with hepatocytes (240-fold), lung cells (11-fold), intestinal cells (5-fold) and kidney cells (2-fold). With bladder cells and fibroblasts, revertant numbers were not significantly higher. We have demonstrated that intact cells, whether or not from the target organ, can metabolize AAF at a high rate to forms which either bind to cellular components or are excreted. These forms are also mutagenic in Salmonella. (no Refs)

12. METABOLIC FATE OF N-METHYL-N-DODECYLNITROSAMINE IN THE RAT, IN RELATION TO ITS CARCINOGENICITY TO THE URINARY BLADDER.

Suzuki E, Mochizuki M, Okada M
Tokyo Biochemical Res. Inst., Takada 3-41-8, Toshima-ku, Tokyo 171, Japan
Gan; 72(5):713-716 1981

The metabolic fate of N-methyl-N-dodecylnitrosamine (MDN) was investigated in the rat, in order to elucidate a possible correlation between urinary metabolites and organotropic carcinogenicity to the urinary bladder of this N-nitrosamine. MDN was extensively metabolized in the rat, no unchanged MDN being found in the urine. The urinary metabolites identified were N-methyl-N-(3-carboxypropyl)nitrosamine (MCPN), N-methyl-N-(2-hydroxy-3-carboxypropyl)nitrosamine, N-methyl-N-(carboxymethyl)nitrosamine, and N-methyl-N-(2-oxopropyl)nitrosamine. Thus the metabolic pattern of MDN was essentially similar to that of N-methyl-N-(4-hydroxybutyl)nitrosamine, a potent bladder carcinogen, in the rat. A possible important role of MCPN in the induction of bladder tumors by MDN is discussed. (Author abstract) (21 Refs)

13. THE MULTIPLE ROLES OF ESTROGEN IN ESTROGEN-DEPENDENT RENAL CLEAR-CELL CARCINOMA OF SYRIAN HAMSTER (MEETING ABSTRACT).

Liehr JG, DaGue BB, Ballatore AM, Sirbasku DA
Department of Biochemistry and Molecular Biology, University of Texas Medical School, Houston, TX, 77025
Growth of Cells in Hormonally Defined Media, September 1-4, 1981, Cold Spring Harbor, New York Cold Spring Harbor Laboratory 101 pp., 1981.

Estrogen (estradiol [E2] or diethylstilbestrol [DES]), when implanted subcutaneously into male Syrian hamster, elicits renal clear-cell carcinoma after approx 6-8 mo. Estrogen alone causes this effect, ie no cocarcinogen is required for tumor initiation or growth response. Studies conducted in our laboratories and elsewhere indicate that the elevated level of estrogen in the hamster results in a variety of different responses and biochemical effects which in a concerted fashion lead to the phenomenon called renal clear-cell carcinoma. Tumor initiation by Estrogen: DES and E2 induce peroxidase activity and microsomal P450 enzymes in a variety of tissues. In turn, peroxidase and microsomal P450 enzymes oxidize DES to a quinoid structure. DES quinone, a chemically unstable and reactive substance, may spontaneously rearrange to beta-dienestrol or, in the vicinity of cellular macromolecules, may covalently bind to DNA. DES-DNA adduct formation was studied in vitro under various conditions. H301 tumor cells, which are derived from the estrogen-dependent renal clear-cell carcinoma of Syrian hamster, remain estrogen-dependent in culture or in host animals. Upon removal of the hormone implant, tumors immediately shrink in size and disappear within 10 days. Estrogen concentration in tumor tissue is low (12-30% of estrogen uptake of liver), despite the presence of estrogen receptors in tumor tissue. (no Refs)

14. METABOLIC ACTIVATION OF DIETHYLSTILBESTROL BY PROSTGLANDIN SYNTHETASE AS A MECHANISM FOR ITS CARCINOGENICITY (MEETING ABSTRACT).

Bennett S, Marshall W, O'Brien PJ
Department of Biochemistry, Memorial University of Newfoundland, Newfoundland, Canada
International Conference on Prostaglandins and Cancer, August 30-September 2, 1981, Washington, DC. Lombardi Cancer Center 75 pp., 1981.

The synthetic estrogen diethylstilbestrol (DES) induces kidney tumors in hamsters and genital tract tumors in rodents. Cervicovaginal alterations including carcinoma were also observed in th e female offspring of DES treated women, as were certain teratogenic changes in the genital tract of their male progeny as a result of its transplacental toxicity. Metzler et al 1978 have suggested that peroxidases of estrogen target organs are responsible by catalyzing DES oxidation to intermediate that bind to nucleic acids and other cellular macromolecules. Our research shows that prostaglandin synthetase could also be a catalyst. Seminal vesicular microsomes and uterine microsomes readily catalyzed the binding of C14 diethylstilbestrol to DNA and protein in the presence of arachidonate but not NADPH. Similar results were obtained with C14 estradiol and could explain the association of estrogens and cancer of tissues whose growth is effected by estrogen. DES also induces liver necrosis in vivo. Blackburn et al 1977 have shown that liver microsomes with NADPH catalyzes the binding of DES to DNA. We have also found that cumene hydroperoxide is much more effective than NADPH in catalyzing this binding. (no Refs)

15. SOURCE OF ARACHIDONIC ACID FOR PROSTAGLANDIN SYNTHESIS IN CANINE KIDNEY CELLS (MEETING ABSTRACT).

Waite M, Daniel LW, Beaudry GA
Bowman Gray School of Medicine, Winston-Salem, NC
International Conference on Prostaglandins and Cancer, August 30-September 2, 1981, Washington, DC. Lombardi Cancer Center 75 pp., 1981.

Madin-Darby canine kidney cells deacylate arachidonic acid from cellular phospholipids in response to stimulation with the cocarcinogen 12-O-tetradecanoyl-phorbol-13-acetate (TPA) and convert the free arachidonate to prostaglandins. We have used this system to determine which phospholipids serve as donors of the free arachidonic acid. The cells were labeled with [3H]arachidonic acid and [14C]palmitic acid which were preferentially incorporated into phosphatidylethanolamine and phosphatidylcholine, respectively. TPA stimulation caused a marked deacylation of [3H]arachidonic acid from several phospholipids including phosphatidylethanolamine, phosphatidylserine, phosphatidylinositol and phosphatidylcholine. 1-Alk-1-enylphosphatidylethanolamine was also a major donor of arachidonate. Some [14C]palmitic acid was converted to palmitoleic and oleic acids that was incorporated into position 2 of the phospholipids. A smaller percentage of [14C] was lost from phospholipids after stimulation, and indicates that the stimulated deacylation of phospholipids is not specific for arachidonic acid. This was confirmed using three other acids that are incorporated into position 2 of phospholipids, linoleic acid and two isomers of eicosatrienoic acid. TPA stimulated the deacylation of all three acids. Only the products from linoleic acid and the isomer of eicosatrienoic acid were converted to prostaglandins; presumably they had been converted to arachidonic acid by chain desaturation and elongation by the cells. (no Refs)

16. PROSTAGLANDIN SYNTHETASE MEDIATED ACTIVATION OF P-DIMETHYLAMINOAZOBENZENE (BUTTER YELLOW) (MEETING ABSTRACT).

Vasdev S, Tsuruta Y, O'Brien P
Department of Biochemistry, Memorial University of Newfoundland, Newfoundland, Canada
International Conference on Prostaglandins and Cancer, August 30-September 2, 1981, Washington, DC. Lombardi Cancer Center 75 pp., 1981.

The oral administration of dimethylaminoazobenzene (DAB) induces rodent liver tumors, mouse lung tumors and dog bladder tumors. It is believed that the activation by the liver of DAB involves liver microsomal mixed function catalyzed sequential N demethylation and N hydroxylation reactions. A cytosolic sulfotransferase then catalyzed the conjugation of the N-OH derivative with sulfate to form an electrophilic species which can bind to nucleic acids and protein. This electrophile is considered to be the ultimate carcinogenic metabolite. An alternative metabolic activation should now be considered. It has been found that prostaglandin synthetase can catalyze the binding of C14 DAB to microsomal protein. Extensive N demethylation occurred and C14 4-methylaminoazobenzene was much more effective at binding to the protein than DAB. Arachidonate was also more effective than NADPH with mouse lung and dog bladder microsomes. Cumene hydroperoxide was also much more effective than NADPH with rat liver microsomes. However, cytochrome P 450 was the catalyst for the latter hydroperoxide reaction as in this case extensive 4'hydroxylation also occurred. (no Refs)

17. PROSTAGLANDIN SYNTHETASE CATALYZED DNA STRAND BREAKS BY AROMATIC AMINES (MEETING ABSTRACT).

Rahimtula A, Moldeus P, Nordenskjoeld M, Andersson B
Memorial University of Newfoundland, Newfoundland, Canada
International Conference on Prostaglandins and Cancer, August 30-September 2, 1981, Washington, DC. Lombardi Cancer Center 75 pp., 1981.

Several aromatic amines are renal medullary toxins and bladder carcinogens. We have found that the aromatic amines 2-naphthylamine, 2-4-diaminotoluene, p aminophenol and p-phenetidine at a concentration of 50uM cause a 2-3 fold increase in DNA strand breaks in cultured human fibroblasts in the presence of sheep vesicular gland microsomes and arachidonic acid. Indomethacin and butylated hydroxyanisole inhibited this reaction. Curiously, benzidine did not give rise to a significant increase in DNA strand breaks. Metabolism of these amines by prostaglandin synthetase was judged by their ability to complete with and inhibit another prostaglandin synthetase dependent reaction - the activation of paracetamol. An 0.1 mM concentration of these amines inhibited the glutathione conjugate formation of paracetamol by 60-90%. Covalent protein binding of [3H]paracetamol was similarly inhibited. At the concentration used, these amines did not significantly affect the cyclooxygenase activity as judged by prostaglandin E2 and prostaglandin F2alpha formation. (2 Refs)

18. PROSTACYCLINS IN PROSTATIC CANCER: A POTENTIAL NON-SPECIFIC TUMOUR MARKER (MEETING ABSTRACT).

Khan O, Hensby CN, Williams G

No affiliation given

International Conference on Prostaglandins and Cancer, August 30-September 2, 1981, Washington, DC. Lombardi Cancer Center 75 pp., 1981.

Prostaglandins have been implicated in many disease states, including the development and spread of malignant tumors. Gas chromatography and mass spectrometry (GC-MC) of prostanoids and their metabolites in various human biological specimens (plasma, urine and benign and malignant tissues) have been analyzed by us. The stable derivative of prostacyclin, (PGI2) is 6-oxo-PGF1alpha was selectively studied. This prostanoid is known to be a potent hormone in inducing bone resorption. In age matched, healthy volunteers, the mean circulating level of 6-oxo-PGF1alpha was 98.5 +/-4.2 picograms/ml, while in patients with a benign prostatic enlargement it was 107.36 +/-8.25 picograms/ml. Whereas, untreated patients with prostatic cancer had a significant increase of 224 +/-3.62 picograms/ml and that in patients with skeletal metastases was even higher. The plasma concentration of 6-oxo-PGF1alpha varied with tumor differentiation and was higher in those patients with a poorly differentiated tumor. These estimations were prior to a rectal examination of the prostate gland. The plasma levels of patients with other tumors (breast, lung, colon, uterus and bladder) prior to treatment were also analyzed and found to be significantly elevated. Painful metastases were associated with raised prostaglandin levels and the biochemical effect of a prostaglandin synthetase inhibitor (Flubiprofen) will be described in over 60 patients. Standard hormonal therapy caused a significant fall in 6-oxo-PGF1alpha levels. Persistently elevated levels were associated with a worsening prognosis. Rising levels correlated with disease progression (by bone scan) and were a more accurate indicator than serum acid phosphatase. (no Refs)

19. CEA, HCG-BETA AND ALPHA-FETOPROTEIN: CLINICAL SIGNIFICANCE OF TUMOR MARKERS.

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Helv Chir Acta; 48(3/4):433-443 1981

The clinical significance of the tumor markers carcinoembryonal antigen (CEA), human choriogonadotropin-beta (HCG-b), and alpha1-fetoprotein (AFP) were studied based on 85 clinical cases and literature. CEA was associated with tumors of the colon, stomach, bronchi, breast, prostate, and bladder, as well as hypernephroid tumors, and was too nonspecific for diagnosis of testicular tumors . Of 19 patients with teratocarcinoma, 57.9% were AFP-positive and 52.6% were HCG-b-positive. Of 38 patients with embryonal carcinoma, 73.7% were AFP-positive and 63.2% were HCG-b-positive. Of 23 patients with seminoma, only 1 (4.4%) was HCG-b-positive. No seminoma patients were AFP-positive. Simultaneous determination of HCG-b and AFP resulted in 85% positive for nonseminoma testicle tumors. Although AFP and HCG-b are not specific enough for marker-oriented therapy, they are important for diagnosis, therapy planning, and case control, and as indicators of metastasis. (29 Refs) (In GER)

20. NEW CLASS OF TRANSFORMING GROWTH FACTORS POTENTIATED BY EPIDERMAL GROWTH FACTOR: ISOLATION FROM NON-NEOPLASTIC TISSUES.

Roberts AB, Anzano MA, Lamb LC, Smith JM, Sporn MB

Lab. Chemoprevention, NCI, NIH, Bethesda, MD, 20205

Proc Natl Acad Sci USA; 78(9,part2):5339-5343 1981

Proteins potentiated by epidermal growth factor (EGF) to induce a transformed phenotype in non-neoplastic rat kidney fibroblasts in cell culture have been isolated from many non-neoplastic tissues of the adult mouse, including submaxillary gland, kidney, liver, muscle, heart, and brain. They resemble previously described transforming growth factors (TGFs) isolated from neoplastic cells as follows: they are extractable by acid/ethanol and are acid-stable, low mol wt (6,000-10,000) polypeptides requiring disulfide bonds for activity, and they cause anchorage-independent growth of non-neoplastic indicator cells that will not grow in soft agar in their absence. Partial purification of these TGFs from submaxillary glands of male mice shows that they are distinct from EGF. Unlike previously described extracellular TGFs, but like certain cellular TGFs from neoplastic cells, they are potentiated by EGF in their ability to promote anchorage-independent growth. The isoelectric point of the submaxillary gland TGF protein is near neutrality. Chromatography on Bio-Gel P-30 followed by high-pressure liquid chromatography has resulted in a 22,000-fold overall purification. The most purified protein is active in inducing growth in soft agar in 1 ng/ml when assayed in the presence of EGF. The data add further evidence to the concept that neoplasia may result from a quantitative, rather than qualitative, alteration in non-neoplastic biochemical processes. (Author abstract) (25 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

21. CONGENITAL MESOBLASTIC NEPHROMA: RELATIONSHIP TO OTHER RENAL TUMORS OF INFANCY.

Snyder HM, Lack EE, Chetty-Baktavizian A, Bauer SB, Colodny AH, Retik AB

Div. Urology, Children's Hosp. Medical Center, 300 Longwood Ave., Boston, MA, 02115

J Urol; 126(4):513-516 1981

Although nephroblastomas (Wilms tumor) do occur in the newborn most of the solid renal tumors in this age group constitute a distinctly different pathologic entity, congenital mesoblastic nephroma. While a more cellular histologic variant of congenital mesoblastic nephroma has been recognized recently, which occasionally may follow a malignant course, the tumor with conventional histology has never been reported to metastasize and follows a benign course when treated by adequate local excision alone. We report our 50-yr experience with 11 cases of this tumor (9 cases with conventional histology and 2 with cellular variant histology). Typically, the tumor presented in the newborn as a large asymptomatic mass. Local invasion was never seen and the tumors were resected without difficulty. Grossly, the tumors rarely exhibited hemorrhage or necrosis. Microscopically, the conventional histologic congenital mesoblastic nephroma was composed of sheets of spindle-shaped

cells. The cellular variant of congenital mesoblastic nephroma exhibited increased cellularity and a higher mitotic index. The relationship of congenital mesoblastic nephromas to other neonatal renal tumors is discussed and a unifying schema of neoplasia in infantile renal tumors is proposed. (Author abstract) (18 Refs)

22. CONGENITAL MESOBLASTIC NEPHROMA.

Gerber A, Gold JH, Bustamante S, Lorch V, Mirza M
(c/o Mirza), Wesley Medical Center, 650 N. Hillside, Wichita, KS, 67214
J Pediatr Surg; 16(5):758-759 1981

Neonatal renal neoplasms are rare; most are congenital mesoblastic nephroma. In the past this neoplasm has been confused with Wilms' tumor, which in part may account for some of the more favorable prognosis ascribed to Wilms' tumor in children less than 1 yr of age. Congenital mesoblastic nephroma is usually a benign tumor. The recommended treatment is surgical excision. This is a report of two cases of congenital mesoblastic nephroma in infants who were treated successfully by nephrectomy. (Author abstract) (6 Refs)

23. ECTOPIC IMMATURE RENAL TISSUE OVER THE DORSUM OF LUMBAR AND SACRAL AREA IN TWO INFANTS AND ITS RELATION TO WILMS' TUMOR (MEETING ABSTRACT).

Posalaky Z, Drake RM, Mawk JR, Franciosi RA
St. Paul-Ramsey Medical Center, St. Paul, MN
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. 92 pp., 1981.

A seven-wk-old female infant was found to have a small, well delineated, sc renal blastema during reparative surgery for meningomyelocele of the lumbar area. A three-mo-old female infant was found to have immature renal tissue, consisting of glomeruli and tubules, in a soft tissue swelling dorsal to the sacrum. Neither of these patients showed neurologic or renal abnormalities. The second patient has had disease-free follow-up period of six yr. The possible origin of these rare findings are considered from misplaced remnants of meso or metanephric tissue, and from under the stimulus of neural plate. The question of whether an immature, ectopic renal tissue in the lumbosacral area could be a precursor to Wilms' tumor is discussed. It seems reasonable to conclude that although these findings are benign, a delayed malignant transformation cannot be ruled out, especially when it occurs in connection with a malformation of distal neural tube. (no Refs)

24. NEW NAMES FOR TWO MAIN GROUPS OF KIDNEY TUMOURS: NEPHROTHELIAL TUMOURS AND NEPHROBLASTEMAL TUMOURS (MEETING ABSTRACT).

Yuryavichus BL
Department of Pathological Anatomy, Vilnius State University, Vilnius, Lithuanian SSR, USSR
Eighth European Congress of Pathology, August 30-September 4, 1981, Helsinki, Finland. The Congress 92 pp., 1981.

On the basis of histopathological, histochemical and electron microscopic studies on more than 500 tumors of the kidney in both adults and children and experimental investigations which include induction of renal tumors in rats by dimethylnitrosamine, new nomenclature is proposed for tumors of the kidney. Hypernephromas or Grawits tumors should be called 'nephrothelial tumors' and divided into two parts: 'adenoma of the kidney' and 'cancer of the kidney'. The group which is well known as Wilms' tumors or nephroblastomas should be called 'nephroblastemal tumors'. (no Refs)

25. NEPHROGENIC ADENOMA OF THE URINARY BLADDER AND URETHRA.

Bhagavan BS, Tiamson EM, Wenk RE, Berger BW, Hamamoto G, Eggleston JC
Dept. Pathology, Sinai Hosp. Baltimore, Baltimore, MD, 21215
Hum Pathol; 12(10):907-916 1981

The histologic and ultrastructural features of nephrogenic adenomas of the urinary bladder and urethra were studied in multiple specimens obtained from eight patients. Three of these were studied by indirect immunofluorescence for Tamm-Horsfall uromucoprotein. The lesions are uncommon benign metaplastic proliferations of urothelium, occurring most frequently in males as small cystic, papillary, or nodular masses and most often presenting with hematuria. Typically the metaplastic tubules resemble nephronic tubules. A florid atypical and pseudoinfiltrative proliferation of these tubules may led to an erroneous diagnosis of adenocarcinoma. Ultrastructural features of proximal convoluted tubules were identified in some of the tubules, but resemblance to specific segments of distal tubules was less certain. The ultrastructural features combined with the absence of Tamm-Horsfall protein in tubular lumina or cells suggest a mesonephric rather than metanephric homology. The lesions are appropriately treated by transurethral resection or fulguration, but persistent lesions were present in three patients up to 18 yr after initial treatment. (Author abstract) (23 Refs)

26. IN VITRO ESTIMATION OF CELL KINETIC PARAMETERS IN HUMAN URINARY BLADDER CANCERS.

Sasaki K, Takahashi M, Ogino T, Yasui H
Dept. Pathology, Yamaguchi Univ. Sch. Medicine, 1144 Kogushi, Ube-shi, Yamaguchi-ken 755, Japan
Gan; 72(5):795-797 1981

The DNA synthetic time (Ts) and the labeling index (LI) of urinary bladder carcinomas from 10 patients were measured by using the 3H-thymidine labeling technique in vitro under hyperbaric oxygen, and the potential doubling time (Tpot) was determined. The LI and Tpot were enormously variable depending on the histologic type, and ranged from 3.7 to 18.0% and from 48 to 136 hr, respectively. In contrast, Ts values fell in a rather narrow range. On comparing these results with the histologic patterns it was found that papillary carcinoma had longer Tpot than nonpapillary carcinoma and histologic grades were not well correlated with the LI's. However, patients with higher LI and/or shorter Tpot showed poor prognosis. The practical significance of these kinetic parameters is discussed. (Author abstract) (13 Refs)

27. REPLACEMENT OF ONE SHEET OF EPITHELIUM BY ANOTHER IN HISTOPHYSIOLOGIC GRADIENT CULTURE, A POSSIBLE SIMULATION OF CARCINOMA-IN-SITU (MEETING ABSTRACT).

Leighton J
Medical College of Pennsylvania, Philadelphia, PA, 19129
In Vitro; 17(3):261 1981

Two epithelial cell lines were put at opposite poles of the circular collagen diaphragm in our histophysiologic gradient culture. Each grew as a sheet on the diaphragm, through which all nutrition reaches the cells. NBT II is a squamous cell carcinoma derived from rat bladder. MDCK is a low grade

adenocarinoma derived from normal dog kidney. In routine propagation each is easily maintained, NBI II reaching confluence more rapidly and requiring more frequent passage. Cultured alone in histophysiologic gradient culture, and studied in living culture by examination of the basal aspect of the epithelium through the transparent collagen membrane, each had its characteristic pattern of tissue organization. When co-inoculated, the sheets met on an irregular front in the middle zone of the diaphragm. In the subsequent week the confluent growth changed as MDCK gradually replaced NBT II. Clusters of NBT II were seen in the fluid-filled cavity of the chamber without attachment to the membrane. One epithelium replaced the other, resembling carcinoma-in-situ. The epithelium with the greater avidity of attachment to the physical-nutritional substrate may be able to undermine and displace the previous occupant. (no Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

28. DISTRIBUTION OF COMMON ACUTE LYMPHOBLASTIC LEUKEMIA ANTIGEN IN NONHEMATOPOIETIC TISSUES.

Metzgar RS, Borowitz MJ, Jones NH, Dowell BL
Dept. Microbiology, Duke Univ. Medical Center, Durham, NC, 27710
J Exp Med; 154(4):1249-1254 1981

The presence of common acute lymphoblastic leukemia antigen (CALLA) in certain c ell types of nonhematopoietic adult and fetal tissues was examined by immunoperoxidase staining with the J-5 monoclonal antibody. Portions of normal tissues were removed during the course of surgery from patients with leukemia or lymphoma and a 20-wk-old fetus was obtained from a prostaglandin-induced abortion. Compared to control ascites fluid from BALB/c mice injected ip with the P3 x 63Ag8 myeloma cell line (P3), no significant staining was found in the fetal heart, liver, lung, pancreas, salivary gland, spleen, or thymus, or in the adult skeletal muscle, spleen, tonsil, salivary gland, small intestine, or colon. However, significant staining was observed in adult kidney, fetal kidney, fetal small intestine, and the myoepithelial cell layer of adult breast. In particular, the J-5 antigen was present on proximal tubules and glomeruli of the kidney. The glomerular staining may have been on the podocyte and not the basement membrane. CALLA was shown to migrate as a 90,000 mol wt antigen rather than the 98,000-100,000 mol wt antigen noted on CALLA-positive tissue culture cell lines. The determinant defined by the J-5 monoclonal antibody may be neither lymphoid cell-specific differentiation antigen nor leukemia-specific antigen. (20 Refs)

29. DEPRESSION OF THE GENERATION OF CELL-MEDIATED CYTOTOXICITY BY MACROPHAGE-LIKE SUPPRESSOR CELLS IN BLADDER CARCINOMA PATIENTS.

Spina CA, Dorey F, Vescera C, Brosman S, Fahey JL
Immunobiology Group, Dept. Microbiology and Immunology, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA. 90024
Cancer Res; 41(11,part1):4324-4330 1981

Depressed T-lymphocyte function as assessed by delayed-type hypersensitivity reactions and in vitro proliferative response to mitogens is a characteristic finding in many types of solid tumors, including bladder carcinoma. Peripheral blood WBC from 16 patients with transitional cell carcinoma of the bladder were compared with age-matched, control subjects. Both the unfractionated WBC containing 10 to 30% monocytes and the lymphocyte-enriched preparations, obtained by monocyte depletion with iron filling ingestion, were analyzed. Mixed WBC culture-induced cytotoxicity was depressed in the patient group; the amount of depression was directly correlated to the extent of the disease. In patients who underwent surgical removal of tumor, the mixed WBC culture-induced cytotoxicity appeared normal. This mixed WBC culture-generated cytotoxic response was a more sensitive indicator of tumor effect than was the induced proliferative response. Removal of phagocytic or adherent monocytes from the responding cell population caused a significant increase in the generated cytotoxicity, especially in those patients with invasive disease. These suppressive effects could be partially reconstituted by quantitative addition of the separated monocytes b ack to the responding lymphocyte culture. The depressed lymphocyte-mediated cytotoxicity present in these bladder cancer patients was due, in a major part, to a circulating macrophage-like cell with active suppressor function. (Author abstract) (39 Refs)

30. SYNTHESIS OF ABH BLOOD GROUP SUBSTANCES IN BLADDER TUMOURS.

Fujita J, Matsumoto K, Kishi K, Ishiyama I
Dept. Urology, Kyoto Univ., Konoe-cho, Yoshida, Sakyo-ku, Kyoto 606, Japan
Br J Urol; 53(5):448-452 1981

A specific red cell adherence test which can detect the cell surface ABH blood group antigens was performed on formalin-fixed frozen sections of 38 bladder tumors. In 27 tumors decreased glycosyltransferase activity was suggested, but the site and the degree of the blockade did not seem to be identical in every tumor. Blood group A and B tumors could be grouped into four types according to the presence of these three isoantigens. One group which showed A or B but no H activity (Type I) consisted only of Grade 1, superficial tumors. All of the invasive tumors belonged to other types. For blood group O tumors no clear-cut correlation could be found between malignancy of the tumor and the presence of H activity. Eight of 22 Grade 2 or 3 tumors and 9 of 21 invasive tumors retained the isoantigen, which seemed to invalidate the use of this test as a predictive indicator. Only where blood group A or B patients were concerned, and the presence of H activity was regarded as abnormal as well as the absence of A and B, could all grade 2 or 3 tumors and all invasive tumors be detected by this test. (Author abstract) (14 Refs)

31. MONOCLONAL ANTIBODIES TO HUMAN PROSTATE AND BLADDER TUMOR ASSOCIATED ANTIGENS (MEETING ABSTRACT).

Starling JJ, Sieg SM, Wright GL
Eastern Virginia Medical School, P.O. Box 1980, Norfolk, VA, 23501
In Vitro; 17(3):224 1981

Monoclonal antibodies to human prostate adenocarcinoma membrane antigens were produced by fusion of spleen cells from BALB/c mice immunized against the prostate adenocarcinoma cell line, DU145, and the P3-X63-Ag8 (P3) myeloma line or the non-secreting 653 variant of the P3 line. The hybrids were screened for antibody production using a solid-phase in vitro binding radioimmunoassy (RIA). Some hybrids produced antibody specific for the immunizing tumor cells and others produced antibody cross-reactive against several tumors, but not normal cell lines. One of these hybrid lines (DU83.21)

secreted antibody that preferentially bound to prostate tumor cells and bladder tumor cells and exhibited weak or no binding to 40 other tumor and normal cell lines tested by RIA. Conventional and competitive binding studies suggest the DU83.21 antibodies do not bind to alpha-fetoprotein, carcinoembryonic antigen, prostatic acid phosphatase, HLA, or DR antigens. Biochemical characterization of the prostate adenocarcinoma membrane antigens is in progress and will be accomplished by immunoprecipitating detergent soluble 125I-labeled cell surface antigens with the DU83.21 monoclonal antibodies followed by sodium dodecyl sulfate gel electrophoresis and autoradiography. (no Refs)

32. STUDIES OF THE ASSOCIATION OF LEUKEMOGENIC AND ONCOGENIC PROPERTIES IN AVIAN LEUKEMIA VIRUSES.

Loliger HC, Von dem Hagen D, Hartmann W
Institut fur Kleintierzucht, Dornbergstrasse 25-27, D-3100 Celle, W. Germany
Haematol Blood Transfus; 26:452-454 1981

Induction of leukocytic and nonleukocytic neoplasias by avian myeloblastosis virus (AMV) and Marek's disease herpes virus (MDHV) was studied in chickens of Leghorn line R (cell types c/O, c/A, and c/AB), Leghorn line M (cell types c/O and c/AB), Leghorn line G (cell type c/B), dysgammaglobulinemic line UM (cell type c/O), and SPAFAS line (cell type c/O). AMV produced leukemia and nephroblastomas in all lines with homozygous cell types c/A, c/B, and c/O, but not c/AB. MDHV induced lymphoid cell reticulosis, but no leukosis, nephroblastomas, or osteosarcomas. Pretumorous lesions of the kidney appeared in 3-wk-old chickens; gross lesions with clinical symptoms appeared between 56 and 112 days after infection, with most appearing after 70 days. Osteopetrosis and osteosarcomas occurred most often in M, UM, and SPAFAS lines. AMV infection was evident in susceptible R, M, and G chickens within 2-5 wk of infection. UM chickens showed aplastic anemia with medullar fibrosis at 12-15 days, followed by stem cell leukemia. SPAFAS chickens showed erythroblastosis first, followed by stem cell leukemia and later by nephroblastomas. The more intense the early hemoblastic disorder was, the lower the chance of development of nonleukocytic neoplasms. (5 Refs)

33. CELLULAR TRANSFORMATION BY BOVINE LEUKEMIA VIRUS (MEETING ABSTRACT).

Amborski GF, Shane BS, Parker S, Butler D
Department of Veterinary Science, Louisiana State University, Baton Rouge, LA, 70803
In Vitro; 17(3):216 1981

Bovine leukemia virus (BLV) transformed cell lines as judged by morphological appearance, growth in reduced serum concentrations and foci formation in soft agar. Infected fetal lamb kidney cells (FLK-BLV) demonstrated foci in monolayer cultures and growth curves showed cellular multiplication in media supplemented with 2, 5 and 10% serum but not with 1%. Less than 1% of the cells grew as colonies in soft agar. Infected bat lung cells (BtLu-BLV) had less discrete foci in monolayer culture, showed similar growth patterns to FLK-BLV with varying serum concentrations but over 90% of the cells grew in soft agar. Although BtLu-BLV cells appeared more highly transformed, the amount of 3H-virus produced by both cell lines appeared similar. The exposure of both cell lines to a mutagen (5-iodo-2-deoxyuridine) did not appear to change th e growth patterns in soft agar, but the level of BLV produced by both cell lines increased. (no Refs)

34. ANTISERUM TO SV40 T ANTIGENS FROM A RABBIT INOCULATED WITH AUTOCHTHONOUS CELLS TRANSFORMED IN VITRO BY SV40.

Tamura H, Shimura H, Kimura G
First Dept. Surgery, Tottori Univ. Sch. Medicine, Nishimachi 36-1, Yonago 683, Japan
Gan; 72(5):769-771 1981

A morphologically transformed cell line was established after infection with SV40 of the primary culture derived from a kidney removed surgically from a rabbit. The transformed cells were free of detectable infectious SV40 particles but produced them upon fusion with permissive monkey cells, and produced SV40-specific large and small T antigens. Repeated sc inoculations of the transformed cells into the animal from which the parental kidney cells had been derived failed to result in tumor formation but raised a substantial level of antibodies to the SV40-specific large and small T antigens as well as to the 58,000 dalton mol wt cellular protein (middle T antigen) (Author abstract) (10 Refs)

REVIEWS AND OTHER RELATED STUDIES

35. BLADDER CANCER AND URINARY CYTOLOGY (MEETING ABSTRACT).

Murphy WM
No affiliation given
Am J Med Technol; 47(5):343 1981

The most recent studies indicate that saccharin is not a risk factor for development of bladder cancer in humans unless large amounts are consumed in conjunction with other factors such as cigarette smoking. After an inauspicious beginning, urinary cytology has established a place in the diagnostic armamentarium of both clinicians and pathologists. Although used to evaluate asymptomatic populations at high risk, urinary cytology is not generally accepted as a screening tool. Its value is in follow-up of patients with previously documented neoplasms and for the detection of carcinoma in situ. The technique is increasingly used to determine the success of chemotherapy. Other uses include evaluation of hormonal status in patients in whom vaginal smears are contraindicated, identification of certain viruses, and early detection of possible allograft rejection. Carcinoma of the urinary bladder exists in two major forms. The majority of tumors are papillary, non-invasive and of low cytologic grade. These have a good prognosis but tend to recur and are associated with frequent hemorrhage. Twenty-five to 30 percent of carcinomas are flat, invasive, of high cytologic grade, and biologically aggressive. Recent developments in urinary cytology allow the differentiation of these two tumor types. Accurate tumor detection often depends upon the type of sample collected, the type of preservation, and the method of processing. Various procedures like carcinoembryonic antigen assays and specific red cell adherence tests have been advocated to aid in the detection of bladder tumors and in the prediction of their biological potential. (no Refs)

36. ESTROGEN- AND ANDROGEN/ESTROGEN-INDUCED AND -DEPENDENT TUMORS IN THE SYRIAN HAMSTER (MEETING ABSTRACT).

Kirkman H
Department of Structural Biology, Division of Human Anatomy, Stanford University School of Medicine, Stanford, CA, 94305
Growth of Cells in Hormonally Defined Media, September 1-4, 1981, Cold Spring Harbor, New York Cold Spring Harbor Laboratory 101 pp., 1981.

The history of, and unanswered questions pertaining to, the following hamster tumors are discussed: estrogen-induced pituitary adenomas and renal carcinomas, androgen/estrogen-induced leiomyosarcomas of the ductus deferens and uterine horn, and similarly induced tumors of the scent gland; the estrogen-induced cystadenomas and carcinomas of the epididymal head, the carcinosarcomas and stromal nodules of the uterine horn, and the possible androgen/estrogen-induced stromal sarcomas of the uterine horn. Discussed also are: the relation of sex hormones to hepatic and mammary gland neoplasia, to fibroangioma and chondroma formation in the external ears, and to adrenal cortical and urinary bladder neoplasia. (no Refs)

37. ROLE OF COBALT, IRON, LEAD, MANGANESE, MERCURY, PLATINUM, SELENIUM, AND TITANIUM IN CARCINOGENESIS.

Kazantzis G
TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Keppel St., London WC1E 7HT, England
Environ Health Perspect; 40:143-161 1981

Experimental, clinical, and epidemiological studies of the carcinogenicity of cobalt, iron, lead, manganese, mercury, platinum, selenium, and titanium are reviewed. Sources of exposure to these metals and their mutagenic effects are discussed. Excess lung cancer mortality has been observed in hematite miners, but occupational exposure to the other metals is not associated with an increased cancer risk. Platinum coordination complexes used in cancer chemotherapy are electrophilic reactants and thus capable of cancer initiation. Cobalt oxide and cobalt sulfate produce injection site and renal tumors in animals, and both are mutagenic. Manganous acetylacetonate and dichlorodicyclopentadienyl titanium also give rise to injection site tumors, but only the latter is mutagenic. Mercury compounds do not appear to be carcinogenic, although some produce genetic damage. The mutagenicity and carcinogenicity of selenium have not been established. (142 Refs)

38. THE SEVEN CANCER WARNING SIGNS RECONSIDERED.

Kahn A
No affiliation given
Med Self Care; 14(2):41 1981

The seven warning signs of cancer are: (1) change in bowel or bladder habits, (2) a sore that does not heal, (3) unusual bleeding or discharge, (4) thickening or lump in the breast or elsewhere, (5) indigestion or difficulty in swallowing, (6) obvious change in wart or mole, and (7) nagging co ugh or hoarseness. For each warning sign, noncancerous conditions with similar symptomatology are presented and discussed. Recommendations on when to seek medical attention are given. (no Refs)

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Zentralinstitut fur Krebsforschung der Akademie der Wissenschaften der DDR, Lindenberger Weg 80, DDR-1115 Berlin, E. Germany
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Environ Health Perspect; 40:93-100 1981

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4. ROLE OF COBALT, IRON, LEAD, MANGANESE, MERCURY, PLATINUM, SELENIUM, AND TITANIUM IN CARCINOGENESIS.
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8. BENZENE AS A RISK FACTOR.
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26. METAL INTERACTIONS IN CARCINOGENESIS: ENHANCEMENT, INHIBITION.
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29. EFFECTS OF METALS IN IN VITRO BIOASSAYS.
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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. HOW HIGH A PERCENTAGE OF ENVIRONMENTALLY RELATED CANCER CASES CAN BE PREVENTED IN NORWAY?.

Langard S
Yrkesmedisinsk avdeling, Telemark sentralsjukehus, 3900 Porsgrunn, Norway
Tidsskr Nor Laegeforen; 101(28):1602-1606 1981

Approx 110,000 cases of cancer were recorded in Norway during the period 1966-1975. Esophageal cancer was diagnosed in 1.099 cases, gastric cancer in 11,702, cancer of the gastrointestinal tract in 9,270, rectal cancer in 4,670, cancer of the liver and bile ducts in 253, pancreatic cancer in 3,992, larynx cancer in 745, lung cancer in 7,608, prostate cancer in 10,835, renal cancer in 3,191, cancer of the bladder and urinary tract in 4,047, and malignant lymphoma in 3,336. The percentage of environmentally related, ie, preventable cancer was estimated after extrapolation to the 1979 incidence. According to the low estimate, 2,250 cases of cancer were attributable to smoking, 300 to alcohol consumption, and 150 to occupational exposure. (15 Refs) (In NOR)

2. TUMOURS IN ICELAND: 3. MALIGNANT TUMORS OF KIDNEY. A HISTOLOGICAL CLASSIFICATION.

Thorhallsson P, Tulinius H
Dept. Pathology, Univ. Iceland, P.O. Box 150, 121 Reykjavik, Iceland
Acta Pathol Microbiol Scand [A]; 89(5):403-410 1981

Malignant tumors of the kidney occurring in Iceland during the yr 1955-1974 were studied pathologically and typed histologically according to a classification proposed, but not yet published, by the World Health Organization. Histological material was available from 89.2% and 84.0% of registered male and female patients respectively. Among males, renal cell carcinomas constituted 91.8%, transitional pelvic carcinomas 5.5% and nephroblastomas 2.7% of classified tumors. The corresponding figures for female were renal cell carcinomas 96.7%, transitional pelvic carcinomas 0.8%, and nephroblastomas 2.5%. The most frequent cell type of renal cell carcinoma group in both sexes was the combination of clear and granular cell, and the most frequent architecture was the combination of solid and tubular patterns. Renal cell carcinomas composed of pure granular cells were found in 22% of males and in 14% of females, and granular cells in combinations with all other cell types were also more common in males. In Iceland renal cell carcinoma is the 5th commonest malignant tumor in males and the 10th in females. The excess of granular cell tumors among males corresponds roughly to, and may account for, the sex difference in the frequency of renal cell carcinomas. (Author abstract) (5 Refs)

3. BLADDER CANCER AFTER SPINAL CORD INJURY. INCIDENCE, PRESENTATION, HISTOLOGY AND PROGNOSIS COMPARED WITH BLADDER CANCER IN THE NON-PARALYSED POPULATION.

El-Masri WS, Fellows G
Natl. Spinal Injuries Centre, Stoke Mandeville Hosp., Aylesbury, Bucks, England
Paraplegia; 19(5):265-270 1981

Twenty-five patients who developed bladder carcinoma were found in the histology records of 6,744 paraplegic and tetraplegic patients. All but four have died of their bladder tumors. While the death rate (per 100,000) for bladder carcinoma in the male population in England and Wales is 7.4, that in the population of 6,744 spinal cord injury patients (taking into consideration age and sex distribution, and length of observation), is 1.1. A quarter of the patients developed their bladder tumors under age 40 yr compared to 3% in the general population. Bladder carcinoma appears to be a long-term complication of spinal cord injury or its management. Fourteen patients were injured between 1940-1949, a decade in which many patients were treated with suprapubic cystotomy (SPC). Lateral wall tumors were found in seven patients. Six patients had anterior wall tumors, three of which arose in the track of a SPC. As to histology, 11 were squamous, and 1 was undifferentiated. Five of the remaining 13 transitional cell tumors were partly squamous. Three of the four long-term survivors had the squamous cell type treated only by radiotherapy (RT); one had a transitional cell carcinoma treated by cystectomy and RT. (5 Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

4. MORTALITY STUDY OF CHEMICAL PLANTS IN THE KANAWHA VALLEY REGION OF WEST VIRGINIA (MEETING ABSTRACT).

Leet TL
No affiliation given
Second Annual NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies, September 9-11, 1981, Rockville, Maryland. National Cancer Institute 33 pp., 1981.

The mortality experience of Union Carbide employees at three chemical plants in the Kanawha River Valley region of West Virginia will be evaluated in a study jointly conducted by the National Institute for Occupational Safety and Health (NIOSH) and the Union Carbide Corporation. These plants have produced many chemicals, including acrylonitrile, ethylene oxide, polycyclic aromatic hydrocarbons (PAH), vinyl resins, and pesticides. A company-sponsored proportionate mortality study based on 819 deaths known to Union Carbide found excess proportions of multiple myeloma and cancer of the kidney and CNS. Initial analyses will evaluate the validity of the apparent excesses as well as evaluate all other cause-specific mortality. Further analyses will test the epidemiologic association between 1) ethylene oxide exposure and leukemia and 2) PAH exposure in the coal hydrogenation process and cancer of the respiratory system, urogenital system, and skin. The study cohort includes approx 44,000 employees who were ever employed by Union Carbide in the Kanawha Valley between January 1, 1940 and December 31, 1978. Demographic and work history data have been coded, keypunched, and computerized for 10,000 active and 34,000 former employees. Vital status ascertainment has been initiated and death certificates are being collected for 6,800 (estimated) deceased employees. (no Refs)

5. ROLE OF GENETIC DISORDERS IN THE DEVELOPMENT OF WILMS' TUMOR.

Sporny S
Zaklad Anatomii Patologicznej, Instytut Patologii AM, ul. Srebrzynska 81 m. 6, 94-209 Lodz, Poland
Wiad Lek; 34(10):835-838 1981

Studies on Wilm's tumor in children show the possible role of genetic factors in the genesis of this tumor. The incidence of developmental malformations of the urinary tract is higher among children with Wilms' tumor than in normal children. Children with Wilms' tumor are also predisposed to other tumors. (16 Refs) (In POL)

6. BLADDER CANCER EPIDEMIOLOGY.

Matanoski GM, Elliott EA
Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 North Wolfe St., Baltimore, MD, 21205
Epidemiol Rev; 3:203-229 1981

Well-known risk factors for bladder cancer are reviewed briefly; unresolved aspects of bladder cancer epidemiology are explored. Topics include mortality and incidence rates (international comparisons, demographic and geographic characteristics, time trends, personal characteristics), latency, cell type, and risk factors (smoking, sugar substitutes, coffee drinking, occupations, hair dyes, Schistosoma haematobium, risks in case clusters, viruses, drug use, and other factors and diseases). Published data on age-adjusted death rates for malignant neoplasms of bladder and other urinary organs for selected countries, annual incidence rates for selected cancer registries, age-specific death rates for malignant neoplasms of urinary organs by race and sex, correlation of age-adjusted death rates for malignant neoplasms of bladder and other urinary organs by sex for states, age-adjusted mortality and incidence rates for bladder cancer by sex for white and nonwhite races, association of smoking, coffee consumption, specific chemicals from the dye industry, and occupations with bladder cancer, and descriptive characteristics of studies relating occupation with risk of bladder cancer are presented. (108 Refs)

7. MORTALITY STUDY OF THE PRINTING TRADES (MEETING ABSTRACT).

Stern FB, Nicholson WJ
National Institute for Occupational Safety and Health, Cincinnati, OH
Second Annual NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies, September 9-11, 1981, Rockville, Maryland. National Cancer Institute 33 pp., 1981.

This cohort mortality study was based on all of the 1,769 active, pension or beneficiary journeymen members on the rolls of Local 2 of the International Printing Pressmen and Assistants Union (IPPAU), New York City, as of January 1, 1950. The vital status as of December 31, 1976 was determined for 98.6% of the cohort; 513 (29.0%) were ascertained to be alive, 1,232 (69.6%) were ascertained to be deceased, the remaining 24 (1.4%) were lost to follow-up. Cause of death information was available for all but 11 (0.9%) deaths. The causes were coded according to the classification of deaths in effect at the time of death. The expected numbers of cause-specific deaths were calculated using age- and calendar yr-specific mortality rates of New York City (NYC) and US white males. A significant excess of total mortality over that of e xpected, either by NYC or US rates, was observed. The important causes of cancer mortality contributing to this excess based on NYC rates were cancer of the buccal cavity and pharynx, prostatic cancer and lung cancer. Based on US rates, the important causes of cancer mortality contributing to the overall excess mortality were cancer of the buccal cavity and pharynx, bladder cancer, all other cancer and lung cancer. An adjustment for possible excessive smoking habits of the cohort did not eliminate the entire mortality excess from lung cancer, cancer of the buccal cavity and pharynx, and prostatic cancer. (no Refs)

8. NITRATE CONTENT OF DRINKING WATER AND MALIGNANT TUMORS OF THE DIGESTIVE ORGANS AND URINARY BLADDER.

Takacs S, Gomori A
Borsod megyei Kozegeszsegugyi-Jarvanyugyi Allmoas, Miskolc, Hungary
Egeszsegtudomany; 25(3):235-247 1981

Relationships between the av nitrate content in drinking water and the incidence of malignant tumors of the esophagus, stomach, large intestine, liver, rectum, and urinary bladder were studied on the basis of 2,755 cases reported during the period 1953-1980 from seven townships and five towns in a country in Hungary. There have been no appreciable changes in the nitrate levels in drinking water during the investigation period. The incidences (per 100,000 population) were 24.4 in men and 5.67 in women for esophageal tumors, 421.9 in men and 202.9 in women for gastric tumors, 84.6 in men and 78.7 in women for tumors of the large intestine, and 102.8 in men and 77.1 in women for rectal tumors. Patients in the age bracket under 40 yr accounted for 4.1% of all cases, patients in the age bracket 40-59 yr for 27.5%, and patients older than 60 yr for 68.4%. The nitrate level in the drinking water exceeded 100 mg/liter for 68.6-72.1% of the patients with digestive tract tumors, and for 54.7% of the patients with bladder tumors. The incidence of digestive tract tumors was highest at nitrate levels in the range of 100-200 mg/liter (-3.4-43%). The findings call for further epidemiological and physiological investigations. (15 Refs) (In HUN)

9. A COHORT STUDY ON CANCER AMONG WORKERS EXPOSED TO AN ANTIRUST OIL.

Jarvholm B, Lavenius B
Dept. Occupational Medicine, Sahlgrenska Sjukhuset, S-413 45 Goteborg, Sweden
Scand J Work Environ Health; 7(3):179-184 1981

An epidemiologic study of workers in an engineering company was conducted following the observation of three cases of cancer among women who wrapped bearing rings covered with antirust oil. Group A (98 persons) worked in the same packing department as the three affected women between 1954 and 1957 and were exposed to white spirit, mineral oil, lanolin, zinc naphthenate, and N-phenyl-1-naphthylamine + sodium nitrite. Group B (33) worked in another packing department and were exposed to mineral oil, vaseline, and stearic acid + sodium nitrite. Group C (31) had been treated for eczema from antirust oil in 1955 and had been exposed to white spirit, mineral oil, lanolin, zinc naphthenate, and N-phenyl-1-naphthylamine. Twelve cancers were found only among the women in Group A (expected value was 3.9 cancers); four cancers each were found in Group B and C (expected values were 2 and 3.8, respectively). The cancers in Group A were in the colon, breast, collum of the uterus (4), ovary (2), bladder, brain, thyroid, and reticulosarcoma. Two workers in Group C developed cancer of the bladder, one of whom was also included in Group A. The most likely etiological agent for Group A can-

cers is N-phenyl-1-naphthylamine, either alone or in combination with sodium nitrite. (15 Refs)

10. RADIATION-INDUCED BLADDER CANCER (MEETING ABSTRACT).

Kennedy DR
Royals Women's Hospital, Melbourne, Victoria, Australia
Br J Urol; 53(1):74 1981

A series of patients irradiated for cervical cancer between 1959 and 1969 and followed for 10 to 20 yr is reviewed. Eight hundred and seventy-three patients were treated and of these 331 survived 10 yr or more. In this latter group 4 patients developed a primary bladder carcinoma after a latent period varying between 11 and 16 yr. The annual incidence rate of bladder cancer in the female population is 4.9/100,000. The exposed population at risk is 4905 person yr. Therefore the expected number of cases is 0.240. The observed number is 4 and is 17 x greater than expected. This figure is statistically significant. Hematuria following radiation treatment for carcinoma of the cervix is usually due to vesical telangiectasia. Since it may occasionally be due to a bladder tumor, all such cases should be fully investigated and cystoscopy should be repeated if bleeding recurs. (no Refs)

11. FAMILIAL AGGREGATION OF UROTHELIAL CARCINOMA.

Mahboubi AO, Ahlvin RC, Mahboubi EO
(c/o E. Mahboubi) Eppley Inst. Res. Cancer, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
J Urol; 126(5):691-692 1981

Reports of unusual clinical cases in the medical literature have contributed to our understanding of the disease spectrum, especially with regard to cancer and exposure to suspected environmental factors. It was projected that in 1980 there would be 35,500 newly diagnosed bladder cancer cases in the United States, which would be the cause of approx 5% of all cancer deaths in male subjects. There are few reports on bladder cancer of familial susceptibility and genetic predisposition, with only four such families described in the literature. We report on a rural family with three cases of transitional cell carcinoma in two generations. (Author abstract) (14 Refs)

12. TOWARDS A STRATEGY FOR THE DETECTION OF INDUSTRIAL CARCINOGENS.

Acheson ED
MRC Environmental Epidemiology Unit, Southampton General Hosp., Southampton SO9 4XY, England
Br J Cancer; 44(3):321-331 1981

Various approaches to the detection of undisclosed occupational carcinogens are outlined. It is emphasized that the screening for carcinogens in the workplace should include evaluation of the time patterns in the incidence of cancer, analysis of the geographic patterns, retrospective analysis of occupational histories of cancer patients, and estimation of cancer risk in exposed populations. The usefulness of these approaches is illustrated by the correlation of standardized mortality rates from bladder cancer to the distribution of the chemical industry in England and Wales. (23 Refs)

13. CHRONIC TOXICITY AND RISK ASSESSMENT IN MICE EXPOSED TO BENZIDINE DIHYDROCHLORIDE (MEETING ABSTRACT).

Littlefield NA, Nelson CJ, Schieferstein G
National Center for Toxicological Research, Jefferson, AR
Toxicologist; 1(1):129 1981

Benzidine, recognized as a bladder carcinogen in man and as a liver carcinogen in experimental animals, is the chemical basis of as many as 200 commercial dyes. It has recently been demonstrated that physiological processes can metabolize these dyes to release benzidine, thereby creating a potential exposure hazard. To assess this hazard, both sexes of F1 hybrid (homogeneous) and F2 (heterogeneous) mice from a BALB/c male and C57BL/6 female cross were exposed for their respective live spans to benzidine dihydrochloride in their drinking water at concentrations of 0, 30, 40, 60, 80, 120, and 160 ppm for males and 20, 30, 40, 60, 80, and 120 ppm for females. Animals were removed from the study only when they were dead or moribund. This study was terminated after 33 mo of exposure. Using the endpoint of hepatocellular adenomas and carcinomas, the Armitage-Doll multistage model was used to describe the tumor rates in the experimental dose range and obtain the upper confidence level on tumor rates. Linear interpolation was used between 0 dose and the upper confidence level of the lowest experimental dosage for predicting potential low dose tumor rates. Dose response effects on body wt, survival, and liver neoplasms were noted in both strains. For each of the endpoints, the females were more susceptible than males and the F1 (homogeneous) strain was more susceptible than the F2 (heterogeneous) strain. The calculated virtually 'safe' dose predicted to produce less than one per million F1 female mice with a liver tumor is 0.04 ppb. One ppb of benzidine dihydrochloride in the drinking water of these mice would theoretically produce liver tumors in less than 2.49 mice per 100,000 population. (no Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

14. RADIATION CARCINOGENESIS. COMPREHENSIVE FINAL REPORT, 16 MAY 1979-31 DECEMBER 19 80.

Warren S, Brown CE, Gates O
Cancer Res. Inst., New England Deaconess Hosp., Boston, MA
Radiation Carcinogenesis. Comprehensive Final Report, 16 May 1979-31 December 1980. Available from National Technical Information Service, Springfield, VA, as DOE/EV/03017-43:, 29 pp., 1981.

This abstract covers three main areas of investigation: mesothelioma induction by asbestos, radiation tumorigenesis and transplantable tumors. Canadian and Rhodesian asbestos fibers have been administered under anesthesia to rats by intratracheal, intrapleural and ip injection. Additional groups were given 3-methylcholanthrene or x-radiation along with asbestos. A large series of mice also treated as above have displayed mesotheliomas. In addition, glass fiber injections and feeding of asbestos were done and have produced negative results to date. The carcinogenic effect of whole-body radiation on hemi-irradiated parabiont partners exposed to a single 1,000 R dose of x-ray was evidenced by a significant increase in the incidence of malignant tumors in only six tissues: skin, supporting soft tissue, kidney, bone, pancreatic islets and ovary. In the male adrenal medulla and in the female breast genetic and parabiotic hormonal factors were judged to exert a significant effect. The

occurrence of incisional (anastomotic) sarcomas in significant numbers in hemi-irradiated and parabiont control pairs suggests the operation of mechanical factors complicating the healing process, only slightly enhanced by radiation. One of the very valuable but unanticipated developments of the rat radiation program was the isolation of two transplantable endocrine tumors with strong hormonal potentials: an insulinoma of the pancreas and a pheochromocytoma of the adrenal medulla. (Author abstract)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

15. INHIBITORY EFFECT OF 4,4'-DIAMINODIPHENYLMETHANE ON LIVER, KIDNEY AND BLADDER CARCINOGENESIS IN RATS INGESTING N-ETHYL-N-HYDROXYETHYLNITROSAMINE OR N-BUTYL-N-(4-HYDROXYBUTYL)NITROSAMINE.

Fukushima S, Hirose M, Hagiwara A, Hasegawa R, Ito N
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
Carcinogenesis; 2(10):1033-1037 1981

Effects of 4,4'-diaminodiphenylmethane (DDPM) in the 'post-initiation' stage of liver, kidney, and bladder carcinogenesis induced in male F344 rats by N-ethyl-N-hydroxyethylnitrosamine (EHEN) or by N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) were investigated. Rats given 0.1% EHEN in drinking water for 2 wk followed by DDPM treatment (0.1% in diet, 32 wk) had significantly fewer renal neoplastic nodules (av 0 28/square cm [cm2]) and renal cell tumors (av 0.16/cm2) than rats treated with EHEN alone (1.88 neoplastic nodules and 0.51 renal cell tumors/cm2). DDPM did not inhibit development of hyp erplastic nodules in the liver. However, hepatocellular carcinomas did not occur in rats treated with EHEN and DDPM, whereas they were observed in 7/21 rats treated with EHEN alone. DDPM (0.1% in diet, 34 wk) also reduced the frequency of bladder papillomas induced by 4 wk or BBN treatment (0.01% in drinking water). In these experiments, rats treated with DDPM showed growth retardation and decreased food intake. (25 Refs)

16. BIOINTERACTION OF SODIUM SELENITE AND AFLATOXIN B1 IN THE MONGOLIAN GERBIL.

Lalor JH, Llewellyn GC
(c/o Llewellyn) Life Science Building, Virginia Commonwealth Univ., 816-822 Park Ave., Richmond, VA, 23284
J Toxicol Environ Health; 8(3):387-400 1981

Mongolian gerbils were fed diets over a 12-wk period containing one of the following: sodium selenite (SSN: 5.0 ppm), aflatoxin B1 (AFB: 12.8 ppm), or SSN (5.0 ppm) + AFB (12.8 ppm). Controls received commercial Chow. All four groups of animals exhibited significant wt gains, but the gain of those treated with SSN + AFB was significantly less than that in the control group. Both groups treated with AFB drank less water/g body wt than did controls during the first 6 wk. Weekly physical activity analysis showed that the group treated with SSN + AFB was significantly more active than all other groups after 5 wk. Relative to control and SSN groups, the AFB group had lower mean liver, kidney, and lung wt. The SSN + AFB group had decreased liver wt but not kidney or lung wt relative to controls. Histopathological damage was limited primarily to liver and kidney in the three test groups. Gastrointestinal pathology was observed only in the SSN + AFB group. Blood analysis showed no change in total leukocytes, but the relative percentage of lymphocytes increased and of neutrophils decreased concurrently in the order: controls less than AFB less than SSN + AFB less than SSN. Hepatic protein analysis revealed two protein peaks in the SSN + AFB group that were absent in all other groups. The proteins may be selenoproteins which are directly or indirectly involved in the lower incidence of histopathological damage in this group. (41 Refs)

17. CARCINOGENICITY OF INHALED 1,2-DIBROMOETHANE IN RATS TREATED WITH DISULFIRAM (MEETING ABSTRACT).

Wong LC, Winston JM, Hong CB
Midwest Research Institute, Kansas City, MO
Toxicologist; 1(1):130 1981

A chronic inhalation study of ethylene dibromide (EDB) was conducted in Sprague Dawley rats. The study consisted of four groups of rats receiving control air and control diet, 20 ppm of EDB and control diet, control air and 0.05% of disulfiram (DS) in the diet, and 20 ppm of EDB and 0.05% of DS in the diet, over a period of 18 mo. Rats receiving 20 ppm of EDB showed high mortality and an increase in tumor incidences in mammary glands, spleen, adrenals, liver, kidneys, and sc tissues. A combination of 20 ppm of EDB and 0.05% DS in the diet caused earlier deaths and high mortality rate, decreases in body wt gain, food consumption, Hb, hematocrit and RBC counts in rats. This combination of EDB and DS treatment also caused early development and high incidences of tumors in liver, spleen, kidneys, adrenals, thyroids, lungs, mesentary and mammary tumors. In addition, 90% of male rats that received a combination of EDB and DS treatment had testicular atrophy. Addition of DS treatment caused early deaths and high mortality rate, and promoted not only the tumor incidences in various organs and tissues in both male and female rats, but also the testicular atrophy in rats. (no Refs)

18. THE EFFECT OF DISULFIRAM ON THE CARCINOGENICITY OF 3,2'-DIMETHYL-4-AMINOBIPHENYL IN SYRIAN GOLDEN HAMSTERS AND RATS.

Fiala ES, Weisburger JH, Katayama S, Chandrasekaran V, Williams GM
Naylor Dana Inst. for Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Carcinogenesis; 2(10):965-969 1981

Species differences in 3,2'-dimethyl-4-aminobiphenyl (DMAB) carcinogenicity, which induces mostly bladder tumors in Syrian hamsters and intestinal and breast tumors in rats, were investigated. Groups of male Syrian golden hamsters received sc injections of DMAB weekly for up to 22 mo (total av cumulative dose 555 mg) either alone or simultaneously with disulfiram in the diet. At the tolerated dose of disulfiram (2.5 mg/kg), the overall tumor yield induced by DMAB alone was not affected, but the number of small intestine tumors was reduced and the appearance of bladder and colon cancers was delayed. In two groups of male Charles River rats, weekly sc injection of DMAB (20 mg/kg) for 37 wk (total av cumulative dose 289 or 241 mg) induced primarily intestinal cancers. As in hamsters, addition of disulfiram to the diet of the second group reduced the incidence of small intestine cancers but resulted in the appearance of a small number of bladder cancers. DMAB-treated rats also developed in situ prostatic carcinoma, regard-

less of whether they were treated with or without disulfiram. (19 Refs)

19. THE EFFECT OF PROMOTERS ON BLADDER CANCER INCIDENCE IN EXPERIMENTAL ANIMAL MODELS (MEETING ABSTRACT).

Hicks RM
Middlesex Hospital Medical School, London, England
International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Multistage models of carcinogenesis have been proposed to account for the observed patterns of tumor development in the skin, liver, lung, bladder and other organs. Such models involve initiation of neoplastic change in a few cells by a threshold dose of carcinogen, followed by conversion of these latent tumor cells into an autonomous cancer by further doses of the same and/or other carcinogens, and/or non-carcinogenic promoting agents. In the rat urinary bladder neoplastic change can be initiated by a few wk treatment with low doses of N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) or N-(4-(5-nitro-2-furyl)-2-thiazolyl)formamide (FANFT) or by a single, low dose, intravesicular instillation of N-methyl-N-nitrosourea (MNU). Very few of the animals treated in such a way will develop bladder cancer in their natural life span unless, in addition, they are exposed subsequently to some further regime which will promote tumor growth from the initiated tumor cells. Many different factors will promote tumor growth in the initiated rat bladder including further low doses of complete bladder carcinogens, some dietary factors such as metabolites of tryptophan or deficiency of vitamin A, the food additives saccharin and cyclamate, and some alkylating agents such as cyclophosphamide and methylmethanesulphonate. Although promoters do not necessarily have all the attributes of complete carcinogens, and may not be mutagenic, by accelerating the process of tumor development and thus lowering the age-related cancer incidence in any particular population they may be of prime importance in regulating overall cancer statistics. (no Refs)

20. PROMOTION IN URINARY BLADDER CARCINOGENESIS (MEETING ABSTRACT).

Cohen SM
University of Nebraska College of Medicine, Omaha, NE
International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Aromatic amines, including, 2-naphthylamine, 4-aminobiphenyl, and benzidine, are known urinary bladder carcinogens in man and other species, but in rodents, aromatic amines and amides have usually induced liver tumors, occasionally also with tumors of the bladder and other tissues. Variations in organ spicificity are related to differences in metabolism; for bladder the rates of acetylation and deacetylation appear to be critical. Bladder specific carcinogens in rodents and other species have subsequently been identified, including N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) administered in the drinking water, N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide (FANFT) in the diet and N-methyl-N-nitrosourea (MNU) instilled intravesically. When low doses of several baldder carcinogens (BBN, FANFT, 2-acetylaminofluorene, and 3,3'-dichlorobenzidine) are administered to rats, either simultaneously or sequentially, a synergistic effect is observed with respect to bladder carcinogenesis. In addition, multistage carcinogenesis has been demonstrated in rats for the bladder using MNU or FANFT as initiators, and sodium saccharin, sodium cyclamate, or tryptophan in the diet as promoters. The urothelium normally has a very low mitotic rate. If mucosal proliferation is increased, such as during fetal development or during r egeneration and repair of an ulcer, the bladder appears to be considerably more sensitive to the effects of promoting substances. For example, if sodium saccharin is administered to rats after ulceration of the bladder, even without prior administration of an initiator, bladder carcinoma develops. Under these conditions, the substance appears as a carcinogen. Human populations with increased bladder epithelial proliferation, such as the fetus, infants, patients with bacterial cystitis, or men with partially obstructive prostatism, may have increased susceptibility to the action of carcinogenic or promoting stimuli. (no Refs)

21. EFFECTS OF PROMOTERS ON N-BUTYL-N-(4-HYDROXYBUTYL) NITROSAMINE INDUCED BLADDER CARCINOGENESIS IN THE RAT (MEETING ABSTRACT).

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International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Male F344 rats were initially given 0.01% N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) for 4 wk in drinking water followed by the feeding of diet containing various chemicals for 32 or 34 wk. In the groups of animals subjected to sodium saccharin, sodium ascorbate, D,L-tryptophan and allopurinol, there was a significant increase in the incidence and number of papillary or nodular hyperplasias (PNH) compared to the groups given BBN alone. However, these compounds did not enhance the induction of papillomas which were generally considered to be more advanced lesions. Experiments were done to determine whether treatment with sodium saccharin or phenobarbital could enhance the neoplastic lesions in the bladder or liver of rats pretreated with 2-acetylaminofluorene (2-AAF) or BBN for initiation. Male Fischer 344 rats were given 0.05% phenobarbital and 5.0% sodium saccharin, respectively for 32 wk after 4 wk administration of hepatocarcinogenesis. Sodium saccharin significantly enhanced the induction of PHN in the bladder, but not of papillomas after BBN treatment, and significantly induced bladder hyperplasias after 2-AAF treatment. However, after 2-AAF or BBN treatment, an effect of phenobarbital for bladder and of sodium saccharin for liver neoplasia induction was not observed. The data indicate that although 2-AAF and BBN have tumor-initiating effects in both liver and urinary bladder, the tumor-promoting effects of phenobarbital and sodium saccharin are organ specific. (no Refs)

22. EFFECTS OF RAT URINE FRACTIONATED BY MOLECULAR WEIGHT ON URINARY BLADDER CARCINOGENESIS.

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Cancer Res; 42(1):15-18 1982

Experimental evidence suggests that rat urine plays a dual role in urinary bladd er carcinogenesis, as a carrier of carcinogen(s) and an enhancer (or promoter) of carcinogenesis in carcinogen-initiated cells. The present experiment was conducted to determine whether -tumor-enhancing activity exhibited by the whole urine resides in a specific fraction(s) when separated by mol wt. Normal rat urine after preliminary filtration to remove gross debris was filtered through Amicon Diaflo membranes to obtain two types of filtrate, one at an ex-

clusion level of mol wt 1,000 and the second at an exclusion level of mol wt 50,000. These filtrates were tested for tumor-enhancing activity in the heterotopically transplanted rat urinary bladders (HTBs) removed from rats pretreated with the carcinogen N-butyl-N-(4-hydroxybutyl)nitrosamine in drinking water for 4 or 10 wk. the incidences of cancer in HTBs receiving repeated instillations of the filtrate at mol wt 50,000 did not differ significantly from those of the HTBs receiving whole urine but were significantly higher than those of the HTBs receiving the filtrate at mol wt 1,000. In the HTBs, which had been exposed to the carcinogen for a longer period of time (10 wk), the filtrate at mol wt 1,000, enhanced the bladder tumorigenesis over that of the osmolality control. The results indicate that there may be two classes of tumor-enhancing activity: the first and major one being in the fraction above mol wt 1,000; and a second one being below mol wt 1,000. the latter fraction appears to exert its effects only on the cells which are in an advanced stage of carcinogenesis. (Author abstract) (10 Refs)

23. EFFECT OF REGENERATIVE HYPERPLASIA ON THE URINARY BLADDER: CARCINOGENICITY OF SODIUM SACCHARIN AND N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]FORMAMIDE.

Cohen SM, Murasaki G, Fukushima S, Greenfield RE
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Cancer Res; 42(1):65-71 1982

The effect of ulceration of the urinary bladder or bladder carcinogenesis induced by N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide (FANFT) or sodium saccharin was evaluated in 5-wk-old F344 rats which were all killed 2 yr after the start of the experiment. The results indicate that long-term feeding of sodium saccharin, a nonmutagen, appears to be capable of inducing bladder tumors if administered to a rat with a proliferating bladder mucosa even without FANFT 'initiation.' Ulceration was induced by freezing. FANFT was fed at a level of 0.2% of the diet for 2 wk, and sodium saccharin was fed as 5% of the diet for 102 or 104 wk. Ulceration followed immediately by FANFT administration and then by control diet for 102 wk did not result in bladder tumors, whereas FANFT administration followed by ulceration and then control diet for a similar period induced bladder tumors. Ulceration followed by FANFT administration and then by 102 wk of sodium saccharin feeding induced bladder tumors, but ulceration followed by 2 wk of control diet followed by 102 wk of sodium saccharin feeding induced a similar incidence of tumors. Ulceration followed immediately by sodium saccharin (fed for 104 wk) induced a slightly lower incidence of tumors. FANFT followed by sodium saccharin without ulceration induced a single bladder carcinoma, but either chemical alone did not induce bladder tumors. Ulceration of the urinary bladder produced by a single ip injection of cyclophosphamide (100 mg/kg) gave similar results as ulceration by freezing. Ulceration alone induced by freezing or cyclophosphamide was followed by a reversible, regenerative nodular and papillary hyperplasia, and the bladder mucosa returned to normal in 3 to 4 wk after ulceration and remained normal through 2 yr. The lack of enhancing effect of FANFT, a potent mutagen, compared to control diet and ulceration induced by cyclophosphamide, a mutagenic alkylating agent, compared to ulceration induced by freezing support the hypothesis of carcinogenesis occurring without mutation. These results may also help to explain the carcinogenicity of sodium saccharin in two-generation and pellet implantation experiments and may assist in the identification of populations with increased susceptibility to bladder cancer. (Author abstract) (53 Refs)

24. COMPARISON BETWEEN A PURIFIED AND STANDARD DIET ON FANFT-INDUCED MURINE BLADDER CANCER.

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Dept. Urology, Univ. Tennessee Center Health Sciences, Memphis, TN
Urology; 18(5):482-484 1981

We investigated the effect of two diets containing equal amounts of the carcinogen FANFT on the incidence and induction time of murine bladder carcinoma in mice. At each time interval, the tumor incidence in the mice ingesting a purified, high-cal diet, was equal or greater than the tumor incidence in the animals fed standard mouse chow. The mean animal wt of the mice ingesting the purified diet was consistently higher than that of the mice fed the standard diet. The bladder wt (an index of tumor vol) showed no significant difference between the mice receiving the two diets. Since mice eat to fulfill their caloric requirements, the animals ate less of the purified diet and the cost per mouse per yr was lower. (Author abstract) (6 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

25. MEMBRANE GLYCOPEPTIDES FROM CHEMICALLY TRANSFORMED CELLS: COMPARISON BETWEEN MESENCHYMAL AND EPITHELIAL CELL LINES DERIVED FROM DIMETHYLNITROSAMINE-TREATED RAT KIDNEY.

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Cancer Res; 42(1):39-43 1982

The membrane glycopeptides of normal and chemically transformed malignant cell l ines derived from rat kidney were investigated by gel permeation chromatography. The cell lines, which were metabolically labeled with L-[5,6-3H]fucose or D-[6-3H]glucosamine, were derived from rats treated in vivo with a carcinogenic dose of dimethylnitrosamine to induce both mesenchymal and cortical epithelial tumors in the rat kidney. Among the cell lines examined were: (a) transformed lines of mesenchymal type derived from the rat kidney 2 to 24hr after the dose of carcinogen; (b) mesenchymal tumor cell lines obtained from the dimethylnitrosamine-induced mesenchymal tumors occurring at 7 to 10 mo; (c) a transformed epithelial cell line derived from rat kidney 48 hr after the carcinogenic dose; and (d) an epithelial cell line obtained from a renal adenocarcinoma induced at 10 mo by a dose of diethylnitrosamine. For control comparisons, populations of normal renal epithelium and mesenchyme were cultured selectively from untreated rats. The radioactive glycopeptides of the neoplastic epithelial cell lines (transformed and tumor) displayed a shift to more complex higher-mol-wt glycopeptides when compared with the normal epithelial counterparts. These results were similar to those reported previously for other cell types. In contrast, the neoplastic cell lines of mesenchymal origin lacked higher-mol-wt glycopeptides, displaying patterns that were identical with those of normal renal mesenchymal cells. It is suggested from these results that the membrane glycopeptide alterations characteristic of virus-transformed and other tumor cells are not detected by these techniques in all cell lines transformed by chemical agents. Furthermore, cell lineage within

the same organ may play a role in the observed difference. (Author abstract) (22 Refs)

26. FURTHER INVESTIGATION OF A NOVEL GAMMA-GLUTAMYL TRANSPEPTIDASE IN HUMAN RENAL CARCINOMA (MEETING ABSTRACT).

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Oncodev Biol Med; Abstracts Book,1:51 1981

A novel gamma-glutamyl transpeptidase (GGTP) found in human renal carcinoma was reported in our previous paper. In the present study, we further investigated some enzymic and immunological properties of the novel GGTP. 1) On isoelectric focusing in sucrose density gradient, the novel GGTP was more acidic than the normal kidney enzyme. But after neuraminidase treatment, both enzymes shifted to a more alkaline range and showed a similar pattern. 2) More than 90% of normal kidney GGTP activity passed through concanavalin A (Con A) sepharose column, while that of the novel one was about 60%. After neuraminidase treatment of both enzymes, about 80% of the normal kidney GGTP still passed through Con A-sepharose column, but the novel GGTP bound to Con A-sepharose column in about 75% of its total activity. 3) The inhibition pat terns of both normal kidney GGTP and the novel one by anti-normal kidney GGTP antibody were almost the same. In an Ouchterlony double diffusion test the precipitin lines of the novel GGTP and the normal kidney against anti-normal kidney GGTP antibody fused completely. These data may indicate that the novel GGTP is immunologically identical with the normal kidney enzyme, but that it differs from the latter at least in its sialic acid content and in some other carbohydrate moieties. (no Refs)

27. IN VITRO AND IN VIVO COVALENT BINDING OF THE KIDNEY TOXICANT AND CARCINOGEN TRIS(2,3-DIBROMOPROPYL)-PHOSPHATE.

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Toxicology; 21(4):291-304 1981

Incubation of 3H-tris(2,3-dibromopropyl)-phosphate (TRIS-BP) with rat liver microsomes led to its activation to products which bound covalently to microsomal protein. The reaction was NADPH-dependent, and boiled microsomes yielded no binding. The reaction could be inhibited by nitrogen; carbon monoxide, which inhibits cytochrome P-450-mediated reactions, also reduced binding rates significantly. SKF 525-A and metyrapone, a selective inhibitor of phenobarbital-inducible cytochrome P-450, inhibited TRIS-BP activation. Alpha-napthoflavone, a selective inhibitor of cytochrome P-448, had little effect. Addition of glutathione and N-acetylcysteine markedly inhibited binding, but ascorbic acid did not. Paraoxon, an esterase inhibitor, and 1,1,1-trichloropropene-2,3-epoxide and cyclohexene oxide also were without effect. Rat kidney microsomes were capable of activating TRIS-BP to 8% of the level achieved by rat liver microsomes. Administration of TRIS-BP to rats resulted in considerable binding to kidney proteins, with lesser amounts detected in liver and very little in muscle proteins. Liver microsomes activated TRIS-BP to bind to DNA in vitro, but kidney microsomes did not. (31 Refs)

28. METABOLISM AND DISPOSITION OF TRIS BP IN THE RAT (MEETING ABSTRACT).

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National Institute of Environmental Health Science and National, Toxicology Program Resear Triangle Park, NC, 27709

Toxicologist; 1(1):35 1981

The flame retardant chemical tris (2,3-dibromopropyl)phosphate (Tris BP), has been shown to be carcinogenic in laboratory animals. In an effort to provide additional data on the disposition of Tris BP in laboratory animals the oral and dermal absorption, tissue distribution, metabolism and excretion of 14C-labeled Tris BP have been studied in the rat. The results of these studies indicate that Tris BP is readily absorbed from the gastrointestinal tract and absorbed at an appreciable rate from the skin. Following absorption Tris BP is distributed to all the major tissues, but Tris BP derived radioactivity is most concentrated in liver, blood and kidney. Tris BP is readily metabolized and excreted in the form of several polar metabolites in urine and feces and as CO2 in exhaled air. Six metabolites of Tris BP have been isolated and identified from urine and bile. Excretion of unmetabolized Tris BP is negligible. In vitro studies of Tris BP metabolism have demonstrated that enzymes in liver degrade the parent chemical to the same polar metabolites which were isolated and identified from urine and bile. The enzymes responsible for Tris BP metabolism are concentrated in microsomal and soluble portions of liver homogenates and require NADPH and glutathione, respectively, as cofactors for enzyme activity. (no Refs)

29. RELATIONSHIP OF RAT URINARY METABOLITES OF N-NITROSOMETHYL-N-ALKYLAMINE TO BLADDER CARCINOGENESIS.

Singer GM, Lijinsky W, Buettner L, McClusky GA

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Cancer Res; 41(12):4942-4946 1981

Nitrosomethylalkylamines with chain lengths from C4 (n-butyl-) to C14 (n-tetradecyl-) were each administered to three rats at doses equimolar with 12 mg of the butyl compound. All of the compounds administered to rats at this dose, twice a wk for 30 wk, induced tumors in 100% of the animals. Some of the compounds with even-numbered alkyl chains induced bladder tumors, and a connection was sought with the metabolites of these excreted in urine. The pooled 24-hr urine was extracted with ethyl acetate before and after acidification to provide a neutral fraction and a fraction containing nitrosamino acids. The fraction containing the acids was analyzed by capillary gas chromatography and by gas chromatography-mass spectrometry after esterification with diazomethane; the neutral fraction was analyzed similarly. The principal metabolite of the nitrosamines with odd-numbered chains was found in the acidic fraction and was identified as nitrosomethyl-2-carboxyethylamine. There were several acids in the mixtures derived from the nitrosamines with even-numbered chains, nitrososarcosine and nitrosomethyl-3-carboxypropylamine being the major components. There was no trend in the yields of the nitrosamino acids that could be correlated with the differences in carcinogenic potency between the nitrosamines; the max yield of acids was more than 30% (from the tetradecyl compound). The principal component of the neutral fraction (+-1% of the nitrosomethylalkylamine administered) was nitrosomethyl-2-oxopropylamine. The yield of this compound increased with increasing length of the even-numbered chain nitrosamines. (Author abstract) (14 Refs)

30. MOLECULAR MECHANISMS INVOLVED IN THE BLADDER TOXICITY OF SODIUM ORTHOPHENYLPHENOL (SOPP) (MEETING ABSTRACT).

Reitz RH, Fox TR, Quast JF, Hermann EA, Watanabe PG
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International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

SOPP has been reported to increase urinary tumors in rats. However, OPP (free base) and SOPP failed to produce mutations in 5 strains of Salmonella typhimurium and SOPP did not induce unscheduled DNA synthesis in rat hepatocytes. DNA alkylation was not detected after gavage with 500 mg/kg of OPP or SOPP. These studies suggest little or no genotoxicity for these materials. Animals consuming diets with 2 percent OPP or SOPP were sacrificed after 3, 7, 14, 30, and 90 days. Progressive hyperplasia of bladder epithelium was noted in the SOPP group, but was absent in the OPP group. Focal kidney lesions were observed in the OPP group, but were largely absent in the SOPP group. The metabolism of both OPP and SOPP was dose dependent. Below 150 mg/kg, 90-97 percent of the urinary metabolites were identified as sulfate and glucuronide conjugates, with 3-6 percent oxidation products apparently derived from microsomal (MFO) pathways. Following 500 mg/kg (gavage) or dietary administration (2 percent) or OPP and SOPP, 20-30 percent of the urinary metaboltes were oxidation products. Thus, the production of reactive MFO metabolites may be correlated with the bladder toxicity observed in rats consuming diets containing high levels of SOPP but not observed after low levels of SOPP. The lack of genotoxicity of OPP and SOPP coupled with the dose dependent production of an oxidative metabolite suggests that the toxicity and carcinogenicity may be manifest only at high metabolically saturating doses. (1 Ref)

31. PROSTAGLANDIN HYDROPEROXIDASE-MEDIATED 2-AMINO-4-(5-NITRO-2-FURYL)[14C]THIAZOLE METABOLISM AND NUCLEIC ACID BINDING.

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Cancer Res; 41(12):4961-4966 1981

Prostaglandin hydroperoxide-mediated metabolism and binding of 2-amino-4-(5-nitro-2-furyl)[14C]thiazole ([14C]ANFT) metabolite to nucleic acids and proteins were investigated with rabbit bladder transitional epithelial and solubilized ram seminal vesicle microsomes. Metabolism was assessed by spectrophotometric and radiochemical techniques. Substrate and inhibitor studies are consistent with both metabolism and binding of [14C]ANFT occurring by the prostaglandin hydroperoxidase activity of prostaglandin endoperoxide synthetase. The ratio of the rates of [14C]ANFT product formation is approx 3:7:10 (organic soluble:non-trichloroacetic acid precipitable: trichloroacetic acid precipitable) over a wide range of arachidonic acid concentrations. Approx 2 and 1% of the total [14C]ANFT metabolized binds to transfer RNA and DNA, respectively. The metabolite isolated from the organic phase had a chromatographic profile and UV spectra different from authentic ANFT. If transfer RNA or DNA is added at the end of a 5-min incubation, no binding to nucleic acids was observed. The demonstration of prostaglandin hydroperoxidase-mediated covalent binding to nucleic acids is consistent with the involvement of this enzyme in 5-nitrofuran-induced bladder carcinogenesis. (Author abstract) (44 Refs)

32. PLASMA LIPID BOUND SIALIC ACID IN PATIENTS WITH PROSTATE AND BLADDER CANCER.

Dunzendorfer U, Katopodis N, Dnistrian AM, Stock CC, Schwartz MK, Whitmore WF
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Invest Urol; 19(3):194-196 1981

Plasma lipid bound sialic acid (LSA) was measured in patients with prostate and bladder cancer to determine the usefulness of this biochemical marker in the staging of malignant disease and in monitoring the efficacy of therapy. Patients with advanced stages of prostate cancer with bone metastases exhibited LSA levels significantly higher than normal subjects. Patients with bladder cancer showed elevations in LSA both in early noninvasive and in advanced stages of the disease. In both types of cancer, patients treated successfully and clinically free of disease did not have elevated LSA levels, whereas patients failing to respond to treatment had persistently high values. (Author abstract) (22 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

33. MITOCHONDRIAL ANOMALIES IN RENAL ONCOCYTES INDUCED IN RAT BY N-NITROSOMORPHOLINE.

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Eur J Cell Biol; 25(2):331-339 1981

Renal oncocytes were induced in male Sprague-Dawley rats by oral application of N-nitrosomorpholine (NNM) in concentration of 12 or 50 mg/100 ml drinking water and analyzed by transmission electron microscopy. The oncocytes exhibited mitochondrial anomalies which were very similar to those of human oncocytoma oncocytes. The most striking mitochondrial changes were an unusually large number of the organelles and an excess of the cristae mitochondriales. The shape of the mitochondria varied from round and oval to extremely elongated slender or cup-shaped organelles often piled up to form complex bodies. Rarely large ramifying mitochondria were found. In addition to transversely orientated cristae or tubules the inner mitochondrial membranes frequently formed dense stacks of unusually long cristae often arranged longitudinally. In some mitochondria straight and strictly parallelly arranged neighboring cristae were found to be connected by a paracrystalline array of pillars bridging the mitochondrial matrix. In the majority of oncocytes the mitochondrial matrix contained prominent dense granules (diameter 30-50 nm), but sometimes these were rare or absent. Individual mitochondria of many oncocytes showed membrane-bound deposits of glycogen particles which usually formed rosettes with a diameter of about 80 nm. Partitioned mitochondria were not seen. Often autophagic vacuoles containing portions of degraded mitochondria and dense bodies, probably autophagosomes, were observed. The nature and significance of the oncocytes remains unclear, but we suggest from these and earlier experimental results that oncocytes represent a special type of a neoplastically transformed cell which usually has only a low potential for 'autonomous' growth. Renal oncocytes induced in rats by chemical carcino-

gens appear to be an excellent experimental model for the further investigation of this cell type. (Author abstract) (46 Refs)

34. ALTERATIONS IN GROWTH REQUIREMENTS OF KIDNEY EPITHELIAL CELLS IN DEFINED MEDIUM ASSOCIATED WITH MALIGNANT TRANSFORMATION.

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J Supramol Struct Cell Biochem; 15(1):63-72 1981

Association of changes in growth requirements of kidney epithelial cells with malignant transformation was studied. Madin Darby Canine Kidney (MDKC) and baby mouse kidney (BMK) cell lines were cultured on Medium K-1 (serum-free medium supplemented with insulin, transferrin, prostaglandin E1 (PGE1), triiodothyronine (T3), and hydrocortisone). Both cell types grew on K-1 and responded to the individual supplements. Deletion of any single supplement resulted in decreased culture growth. The fewest MDKC or BMK colonies were found if transferrin or PGE1 was deleted. Results indicated MDKC as a suitable model for normal kidney cells in vitro. Malignant transformation of MDKC by Moloney sarcoma virus resulted in reduction of the optimal dose of insulin and the elimination in some cells of the PGE1 requirement. Transformed cells required fibronectin for growth in K-1. Variant cells were tumorigenic in adult nude mice and had altered cyclic AMP metabolism. (20 Refs)

35. DEVELOPING UROTHELIAL CARCINOMA: ITS CYTOLOGIC FEATURES AND CLINICAL IMPLICATIONS (MEETING ABSTRACT).

Murphy WM, Crabtree W
Department of Pathology, Baptist Memorial Hospital, Memphis, TN
Twenty-ninth Annual Scientific Meeting of the American Society of Cytology, November 2-7, 1981, St. Louis, Missouri. 90 pp., 1981.

Numerous experimental and clinical studies have shown that bladder cancers may grow through precursor stages. These developing lesions have been characterized histologically by examination of biopsied tissue and by complete 'mapping' of resected bladders. Carefully controlled carcinogenesis in various experimental model systems has shown that urothelial carcinoma arises via a series of progressively more severe cellular changes occurring in flat and/or papillary epithelium. Logically, similar events occur in humans but determination of their frequency and order of progression will require observation of a great many patients over several yr. Meanwhile, the morphologic changes of developing urothelial carcinoma must be identified and characterized and specimens harboring such abnormalities must be labeled for future study. In addition, the significance of these changes in a patient population not selected for urothelial carcinoma must be established. To determine the cytologic features most characteristic of developing urothelial carcinoma, we first studied the histologic features of these lesions in three experimental model systems. Using the cytologic criteria thus defined, we sought to document their significance when applied to an unselected hospital and clinic population. For the purpose of this evaluation, both histologic and cytologic changes reflecting the morphologic features determined in the experimental systems were termed 'dysplasia'. Among 1,554 urinary specimens (656 patients), dysplastic cells were the most significant abnormality in 74 (48 patients). Hospital records indicated that 60.5% of these individuals either had or were being followed for cancer, 10.4% had primary dysplasia, and 2.1% urothelial hyperplasia; 27% of patients had other diseases. Among the 34 individuals with tissue documentation, 73.6% had cancer, 14.7% dysplasia, and 2.9% hyperplasia. (no Refs)

36. PRIMARY ADENOCARCINOMAS OF THE HUMAN URINARY BLADDER: HISTOCHEMICAL, IMMUNOLOGICAL AND ULTRASTRUCTURAL STUDIES.

Alroy J, Roganovic D, Banner BF, Jacobs JB, Merk FB, Ucci AA, Kwan PW, Coon JS, Miller AW
Dept. Pathology, Tufts Univ., Sch. Medicine, 136 Harrison Ave., Boston, MA
Virchows Arch [Pathol Anat]; 393(2):165-181 1981

Neoplastic and non-neoplastic tissue specimens from 10 patients with primary adenocarcinoma of the urinary bladder were examined. Most of these tumors were associated with either foci of transitional cell carcinoma and/or with glandular metaplasia of the bladder epithelium. The mucin produced by the neoplastic cells was PAS, alcian blue, mucicarmine, PB/KOH/PAS, and RPB/KOH/PAS-positive. ABH isoantigens of these tumors were not always deleted. Ultrastructurally, the neoplastic cells resembled goblet cells. Their plasma membrane had numerous microvilli with prominent glycocalyx. Proliferation and attenuation of tight junctions were noted. The gap junctions were few and small. Two types of desmosomes were found. The ultrastructural features of the neoplastic cells were attributed in part to the malignant transformation and in part to the direction of their differentiation. We have not observed any distinctive morphologic, histoch emical, immunologic or ultrastructural features that might be diagnostic for these adenocarcinomas. (Author abstract) (53 Refs)

37. TRANSPLANTATION AND CELL CULTURE OF RAT URINARY BLADDER CARCINOMA.

Cohen SM, Yang JP, Jacobs JB, Arai M, Fukushima S, Friedell GH
Dept. Pathology, St. Vincent Hosp., Worcester, MA, 01604
Invest Urol; 19(3):136-141 1981

Six bladder carcinoma cell lines were established in culture from male Fischer rats fed N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide. Five were papillary transitional cell carcinomas by back transplantation and one was squamous. Each has been maintained in culture for more than 4 yr. The light, transmission, and scanning electron microscopic features of the cells in culture and transplantation are described. (Author abstract) (15 Refs)

38. CYTOLOGIC AND HISTOLOGIC FEATURES OF MIXED CARCINOMA OF THE URINARY BLADDER (MEETING ABSTRACT).

Mandell D, Rosenthal DL, Waisman J
Division of Surgical Pathology, University of California Los Angeles School of Medicine, Los Angeles, CA
Twenty-ninth Annual Scientific Meeting of the American Society of Cytology, November 2-7, 1981, St. Louis, Missouri. 90 pp., 1981.

Five patients with mixed carcinomas of the urinary bladder, each with a mixed population of malignant-appearing transitional and glandular cells in the urine and urinary washings are presented. We define mixed carcinomas as having major distinct, and simultaneous neoplastic transitional, glandular, or squamous components; we do not include minor metaplastic elements in this group. Most cancers of the urinary bladder are transitional carcinomas with a varied population of transitional cells in urine and washings of the urinary bladder. Poorly differentiated transitional carcinomas frequently have small areas of squamous and glandular metaplasia; but the cells in the urine

washings reflect the anaplastic character of the tumor, and the minor metaplastic components do not represent a diagnostic problem. Likewise, the pure adenocarcinomas and epidermoid carcinomas of the bladder are readily identified by the presence of large numbers of atypical cells of characteristic differentiation in the urine and in vesical washings. All five of our mixed carcinomas are mixed transitional and adenocarcinomas. The histology and cytology of these tumors will be contrasted with those from unmixed carcinomas of the bladder having squamous and glandular metaplastic components. The mixed carcinomas should be identified by cytologic procedures and confirmed by biopsy so that appropriate therapy can be planned. Mixed carcinomas of the urinary bladder may be more common than supposed and reflect the varied derivation and potential of the cells lining the lower urinary tract. (no Refs)

39. DEMONSTRATION OF HETEROGENEITY IN A CELL LINE FROM A HUMAN UROTHELIAL TUMOUR (ME ETING ABSTRACT).

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Cell Biol Int Rep; 5(SupplA):23 1981

Seven populations of cells were clonally isolated from a human urothelial carcinoma-derived cell line (EJ). The parent cell line had a heterogeneous chromosome constitution and showed a transformed phenotype in that it grew in agar and produced tumors in nude mice. Each clone was chromosomally unique; three clones had a pseudo-diploid chromosome constitution and four had either hypo- or hyper-tetraploid chromosome modes. All seven clones formed colonies in agar, but with widely varying (0.5-9%) efficiencies. Six of the clones produced sc tumors in nude mice. The seventh clone, which had a high colony forming efficiency in agar, did not produce tumors in nude mice, confirming other findings that these two commonly used markers of transformation are not always associated in epithelial cells. The phenotypes of the clones were stable until at least passage number 40 in vitro. Specific chromosome aberrations, detectable by G-banding techniques, were associated with colony forming efficiency and tumorigenicity as previously proposed. (3 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

40. IMMUNOPEROXIDASE STUDIES ON A TUMOR-CELL-ASSOCIATED ANTIGEN(S) IN RAT RENAL NEOPLASMS INDUCED BY DIMETHYLNITROSAMINE.

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Inst. General and Comparative Pathology, Bulgarian Acad. Sciences, Sofia-1113, Bulgaria
Neoplasma; 28(4):447-455 1981

Renal neoplasms were induced in rats of Wistar line by a single, ip injection of dimethylnitrosamine (60 mg/kg). The histological investigation indicated that these tumors were entirely mesenchymal in nature. In some of them (16.6%) small adenocarcinomas were seen. Immunological studies were carried out by light and electron microscope, using the immunoperoxidase 'bridge' technique. Tumor cell-associated antigen(s) was detected in 62% of the neoplasms examined. This antigen was individual as it did not react with sera from the other tumor bearing rats. It was established that this antigen was located mainly on the plasma membrane and also, even though in a lesser degree, on the endoplasmic reticulum and nuclear envelope of the tumor cells of mesenchymal and epithelial origin. Except the existence of tumor cell-associated antigen(s) in these neoplasms, the presence of antibodies produced against them in the sera of the diseased rats were also detected by these investigations. (Author abstract) (23 Refs)

41. THE DISTRIBUTION OF COMMON ALL ANTIGEN (CALLA) IN NON-HEMATOPOIETIC TISSUES (MEETING ABSTRACT).

Metzgar RS, Borowitz M, Jones NH, Dowell BL
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related D iseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

CALLA is defined by polyclonal and monoclonal xenogeneic antisera and is a 100,000 mol wt glycoprotein. We have recently tested the J-5 monoclonal antibody to CALLA on sections of various human adult and fetal tissues by immunoperoxidase staining. The following tissues demonstrated no significant immunohistochemical staining when compared to the P3 ascites control: fetal heart, liver, lung, pancreas, salivary gland, spleen and thymus, and adult skeletal muscle, spleen, tonsil and colon. Certain adult and fetal tissues, however, showed significant staining. In the adult kidney, most but not all the tubules stained intensely. Because of the large number of positive-staining tubules and their lower nuclear density compared to the nonstaining tubules, it appears that the CALLA positive cells are in the proximal tubules. The pattern of staining in the tubules was apical, and sloughed or secreted antigenic material was present in the tubular lumens. In addition to the tubular staining, there was intense glomerular staining in fairly linear pattern along glomerular basement membranes. A similar staining pattern was present in fetal kidney. The fetal small intestine also showed apical staining of the epithelial cells of the villi, with some shedding of antigenic material noted. In contrast, a different pattern of staining was noted in adult breast. Although there was no significant staining of the breast epithelium, or the material within glandular lumens, there was staining around the myoepithelial cell layer of the breast. This was particularly prominent in the breast ducts but was also seen to some extent in the acini of the breast as well. (no Refs)

42. STUDIES ON THE LOCALIZATION OF THE GLYCOPROTEIN GP-2 WITHIN THE RENAL GLOMERULUS IN VIVO AND IN CULTURED KIDNEY CELL STRAINS IN VITRO.

Oberley TD, Chung AE, Murphy-Ullrich JE, Mosher DF
Dept. Pathology, Univ. Wisconsin Medical Sch., Madison, WI
J Histochem Cytochem; 29(11):1237-1242 1981

Positive staining for the glycoprotein GP-2 was demonstrated in the kidney glomerulus by use of the indirect peroxidase-labeled antibody technique. At the ultrastructural level, heaviest staining for GP-2 was demonstrated along the lamina rara externa and lamina rara interna of the glomerular and tubular basement membranes, demonstrating definite molecular organization for structures which appear amorphous even at the electron microscopic level. However, GP-2 was also present in the lamina densa of the glomerular basement membrane, but not of the tubular basement membrane. The staining for GP-2 is in contrast to the predominantly mesangial staining for fibronectin. Using the indirect immunoperoxidase techniques for kidney

cells cultured in vitro, it was demonstrated that cell surfaces of specific subpopulations of g lomerular cells stained heavily for both fibronectin and GP-2, while renal medullary cells did not stain at all using specific antiserum to these molecules. GP-2 was present extracellularly and showed moderate staining in glomerular cell culture, while fibronectin showed heavy staining in this location. (Author abstract) (12 Refs)

43. STUDIES ON T CELL BEARING FC RECEPTORS FOR IGG OF PERIPHERAL LYMPHOCYTES IN PATIENTS WITH BLADDER CARCINOMA.

Shimatani N

Dept. Urology, Kobe Univ. Sch. Medicine, Kobe, Japan

Hinyokika Kiyo; 27(6):637-647 1981

To test the cellular immunocompetence in patients with bladder carcinoma, a study was made on the lymphocyte subpopulation of 34 patients and 35 healthy men. T cell was identified by spontaneous rosette formation with sheep RBC, and B cell was identified by EAC rosette formation. T lymphocytes bearing Fc receptors for IgG (IgGFcR+ T cells) were detected by double rosette formation of neuraminidase treated sheep RBC and glutaraldehyde treated sensitized ox RBC. The percentages of IgGFcR+ T cells in total T cells in peripheral lymphocytes of 35 healthy men and 34 untreated bladder cancer patients were 5.8 +-1.9% and 14.2 +-8.4% respectively, the percentages of T cells in peripheral lymphocytes of 35 healthy men and 34 untreated bladder cancer patients were 81.3 +-6.3% and 68.6 +-14.0% respectively. The difference between these figures was statistically significant. There was a tendency to decrease in percentage and absolute count of T cells in the patients with higher grade and stage of the tumor. Contrary, there was a tendency to increase percentages of IgGFcR+ T cells in total T cells of the patients with higher grade and stage of the tumor. No influence of operation was found on T cell percentage, absolute count of T cell and the percentage of IgGFcR+ T cells in total T cells. Steroids which were secreted by stimulation of operative stress might have an effect on the percentages of IgGFcR+ T cells in total T cells. (Author abstract) (33 Refs) (In JPN)

44. EFFECTOR CELLS IN NATURAL CYTOTOXICITY AGAINST HUMAN BLADDER CANCER CELL LINES.

Bloom ET, Dunsworth-Browne M, Durkos-Smith D

GRECC 691/11G, Veterans Admin. Wadsworth Medical Center, Los Angeles, CA, 90073

Urol Res; 9(5):219-225 1981

Mononuclear cells were obtained from normal donors and from patients with nonmalignant genitourinary diseases, bladder cancer, and other cancers. The cells were tested for cytotoxicity after depletion of Fc-receptor-bearing (FcR+) cells by monolayer immune complex fractionation or the RBC-antiRBC monolayer technique. FcR+ cell depletion significantly decreased cytotoxicity of effector cells (ECs) against transitional cell carcinoma, colon carcinoma, and amnion target cells in a 40-hr assay. No bladder cancer-specific cytotoxicity was detected. Cultured ECs from normal donors were positive for natural killing (NK) against transitional cell carcinoma and amnion cells. The NK activity appeared to involve FcR- T and B cells since FcR+ cells were frequently undetectable. Monocytes did not play a significant role in NK. (21 Refs)

45. IDENTIFICATION BY IMMUNOFLUORESCENCE OF ABO(H) ANTIGENS IN STAGE A BLADDER CARCINOMA. CORRELATION WITH THE CLINICAL COURSE IN 125 CASES (MEETING ABSTRACT).

Pascalis-Augustin I, Le Portz B, Hammou JC, Vacant R, Maiolini R, Deslignieres S, Fella C, Steg A, Masseyeff R

INSERM U 210, 06034 Nice Cedex, France

Oncodev Biol Med; AbstractsBook,1:P22 1981

Conventional microscopic tissue sections of bladder carcinoma, originating from 125 stage A patients, whose clinical courses were followed-up for 5 yr or more, were stained for blood group antigens (BGA) ie A, B and H antigens. A double layer immunofluorescence technique was employed, where the first antiserum was a human anti-A, B or H according to the patient blood group (A: 36.8%, B: 12.0%, AB: 5.6%, O: 45.6%), and the second antiserum a goat anti-human immunoglobulin labelled with fluorescein. The staining patterns were classified in three groups: in group 1, all tumoral cells expressed BGA; in group 2, only a proportion of cells were BGA positive; in group 3, all tumoral cells were BGA negative. Survival rates at 5 yr were 100% in group 1 (11 patients), 38% in group 2 (37 patients) and 27% in group 3. The correlation of the immunofluorescence patterns with the other commonly adopted risk factors was also investigated. This study confirmed the conclusions reached by previous studies using the red adherence test that the deletion of the expression of BGA is associated with an unfavorable clinical evolution. However, the immunofluorescence test was found to be simpler and more reliable, leading to results with a better predictive value. (1 Ref)

46. THE LEUKOCYTE ADHERENCE INHIBITION ASSAY AS A MEASURE OF ANTITUMOR IMMUNITY IN BLADDER CANCER PATIENTS.

Ramsey EW, Malcolm AJ

Dept. Surgery (Urology), Health Sciences Centre, 700 William Ave., Winnipeg, Manitoba, Canada

J Urol; 126(5):600-603 1981

The leukocyte adherence inhibition test was used to assess antitumor immunity of patients with transitional cell carcinoma of the bladder. Patients and controls were tested against extracts of transitional cell carcinoma as well as extracts of renal cell carcinoma and normal bladder mucosa. Patients with transitional cell carcinoma had significantly greater reactivity compared to patients with other genitourinary disease or normal controls. With a pooled tumor extract from six different transitional cell tumors a positive response was obtained in up to 82% of patients with transitional cell carcinoma compared to 12% of patients with other genitourinary disease. These results suggest that the leukocyte adherence inhibi tion test is a sensitive and fairly specific test of antitumor immunity in patients with transitional cell carcinoma of the bladder. (Author abstract) (30 Refs)

REVIEWS AND OTHER RELATED STUDIES

47. CARCINOMA OF THE BLADDER.

Tauber R

Urol. Univ.-Klinik, Klinikum Grosshadern, Marchioninistrasse 15, 8000 Munchen 70, W. Germany

Fortschr Med; 99(40):1630-1636 1981

The occurrence, diagnosis, and treatment of bladder cancer is reviewed. The etiology of such tumors is discussed with regard to the role of carcinogens, such as aromatic amines, and the increased risk of bladder cancer associated with specific occupations, such as those of painters and textile workers. The classification of bladder tumors is described with respect to histological criteria established by the World Health Organization, clinical TNM (tumor, node, metastases) staging and histopathologic P-classification, and various growth forms of the tumors. Symptoms of bladder tumors are outlined, and the value of different diagnostic procedures in correctly assessing TNM stages is considered. Surgical treatment of bladder tumors is discussed; emphasis is placed on factors which influence the choice of the initial surgical procedure and of the procedure to be used with recurrent tumors. Methods, indications, and advantages are described for transurethral resection, partial bladder resection, cystectomy, and urinary diversion following cystectomy. The efficacy of chemotherapy and radiotherapy in the treatment of these tumors is considered. The prognoses for patients with bladder tumors are examined; it is noted that early detection and accurate diagnosis have positive effects on prognosis. (no Refs) (In GER)

48. GENITOURINARY CANCERS.

Qazi R

Rochester Univ. Sch. Medicine and Dentistry, Rochester, NY

Practical Cancer Chemotherapy. Rosenthal SN, and Bennett JM, ed. Garden City, NY, Medical Examination Publishing Co., 461 pp., 1981.

Malignancies of the kidney, bladder, prostate and testes are reviewed in detail. Adenocarcinomas of the kidney comprise about 3% of all malignancies in the United States. A recent report of a family with hereditary renal cell carcinoma provides the first example of a dominantly inherited chromosome aberration which causes a high risk of a specific human malignancy. Surgery is the only curative therapy for renal cell carcinoma, with a 5-yr-survival rate after radical nephrectomy of 60-76%., Bladder cancer accounts for about 4.5% of new cancers in the United States each yr, with transitional cell carcinomas accounting for 90% of the total. Optimal management of high grade invasive bladder cancer consists of radical cystectomy with preoperative radiation therapy. Nevertheless, greater than 50% of treated patients develop distant metastases within 2 yr and require systemic therapy. Because cis-platinum is the most effec tive single agent in bladder cancer, platinum-based combinations are being widely investigated. Adenocarcinoma of the prostate is the third most common cause of cancer death in males, following lung and colorectal cancers. Both surgery and radiation therapy with curative intent are used to treat localized carcinoma of the prostate. Testicular carcinoma accounts for only 1-2% of malignant tumors in males but represents the most common cause of cancer deaths in the 29-35 yr age group. Diagnosis, staging and treatment of the various histologic types of testicular tumors are discussed. (102 Refs)

49. STEROID RECEPTORS IN UROLOGICAL MALIGNANCIES.

Ekman P

Dept. Urology, Huddinge Univ. Hosp., S - 141 86 Huddinge, Sweden

Acta Obstet Gynecol Scand [Suppl]; (101):87-92 1981

Within urological practice, three important types of cancer seem to be under endocrine influence or develop in endocrine-dependent organs: prostate cancer, hypernephroma and testicular tumors. Endocrine therapy is not used in testicular cancer, its value in renal cell carcinoma is limited, whereas it is a dominant form of therapy for prostate cancer. There seems to be a definite relation between androgen receptor content in primary prostatic carcinoma and response to hormonal manipulations. The presence of estrogen receptors is not well documented and probably the major effect of estrogen therapy is indirect, being exerted via the hypothalamo-pituitary axis. Progestin receptors are present in hyperplastic prostate as well as in prostate cancer and may indicate cases sensitive to progestin therapy. The assay method still needs considerable refinement before it can be introduced into clinical practice. (Author abstract) (65 Refs)

50. CYTOCHEMICAL AND BIOCHEMICAL MICROANALYSIS OF CARCINOGENESIS.

Bannasch P, Benner U, Hacker HJ, Klimek F, Mayer D, Moore M, Zerban H

Abteilung fur Cytopathologie, Institut fur Experimentelle Pathologie, Deutsches Krebforschungszentrum, D-6900 Heidelberg 1, W. Germany

Histochem J; 13(5):799-820 1981

The use of analytical cytochemistry, enzyme cytochemistry, autoradiography, microdissection, and biochemical microanalysis in the elucidation of mechanisms of cell transformation is reviewed. The first cytopathologic phenomenon which can be detected by cytochemical means during the process of hepatocarcinogenesis is an excessive storage of glycogen. Hepatocellular glycogenesis is related to the dose and time of carcinogen treatment and to the development of hepatocellular tumors. A sequence of cellular changes has been established leading from the glycogen-rich hepatocyte, which appears clear or acidic in hematoxylin/eosin sections, to the basophilic hepatoma cell, which is poor in glycogen but rich in ribosomes. Excessive storage of polysaccharides or lipids is correlated with the development of other tumors as well, including renal epitheliomas induced in rats by oral application of nitrosomorpholine. Three types of epithelial kidney tumors develop under these conditions, all with specific histogenesis and cytogenesis. Extensive light-, electron- and fluorescent micrographs illustrate the text. (68 Refs)

51. GAMMA-GLUTAMYLTRANSPEPTIDASE: A TUMOR CELL MARKER WITH A PHARMACOLOGIC FUNCTION.

Vanderlaan M, Phares W

Biomedical Sciences Div., Lawrence Livermore Natl. Lab., P.O. Box 5507, Livermore, CA, 94550

Histochem J; 13(5):865-877 1981

The histochemical distribution of gamma-glutamyltranspeptidase (GGTP) in rat and human tissues is reviewed, and the changes observed during embryogenesis and carcinogenesis are discussed. The pattern of GGTP distribution is similar in both species, with activity in adults found primarily in the proximal tubules of the kidney, the secretory follicle cells of the pancreas, and the villous cells of th jejunum. There is only minimal activity in intestinal crypt cells, but consider-

able in mature villus cells. Mammary gland, bile duct cells in adult liver, endothelial cells of brain capillaries, follicle sheath cells in actively growing hairs, and lymphocytes also have associated GGTP activity. Higher activity is seen in both embryonal and cancerous tissues. Soon after initial exposure to carcinogens, islands of presumably preneoplastic cells form in the liver, and are characterized by very high GGTP activity. The majority of hyperplastic nodules and carcinomas that eventually develop also have increased GGTP activity. This induction of increased activity persists long after carcinogen exposure. The possible metabolic significance of GGTP is discussed. (63 Refs)

52. ANAESTHETIC GASES AND HEALTH RISKS TO LABORATORY PERSONNEL: A REVIEW.

Green CJ

Div. Comparative Medicine, Medical Res. Council Clinical Res. Centre, Watford Road, Harrow, HA1 3UJ, England

Lab Anim; 15(4):397-403 1981

The evidence that chronic exposure to inhalational anesthetic agents may be associated with psychomotor, hepatic and renal dysfunction, to increased susceptibility to infections and neoplastic disease, and to an increased incidence of miscarriages and fetal abnormalities, is discussed. The risk to pregnant women seems greatest after exposure to rather high concentrations of nitrous oxide. Although it is not suggested that all laboratory premises will be equally at risk, such levels as 400 ppm halothane and 8,000 ppm nitrous oxide can build up in small poorly-ventilated rooms when these agents are used for several hr at a time. A strong plea is entered for all to be aware of the hazard and to ensure that good ventilation and preferably, purpose-built scavenging equipment are installed wherever inhalational agents are used. (Author abstract) (82 Refs)

53. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.

Kalmaz EV, Kalmaz GD

Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916

Chemosphere; 10(10):1163-1175 1981

Effects of chlorine residuals and organic compounds in drinking water and aquatic environments, particularly direct toxicity and/or carcinogenicity to human and aquatic life, are reviewed. Significant correlations between surface water chlorination and cancer mortality rates have been shown in humans. Elevated rates of bladder, rectal, colon, and gastrointestinal cancers in humans served by chlorinated water from the Mississippi River have been demonstrated. The use of chlorinated surface waters in Ohio was associated with stomach cancer in males and females, and with bladder cancer in males. Chloramine has been shown to be an extremely weak mutagen; involvement of DNA is suggested, since DNA-repair mutants are sensitive to the agent. In uremic patients, shortened RBC survival and hemolysis have been attributed to chlorinated tap water used in hemodialysis. Effects on aquatic life of chlorine residuals are reviewed. While more than 300 chlorinated organic compounds have been identified in chlorinated potable waters, cooling waters, and sanitary effluents, relatively little is known about their ecological effects. Laboratory research using animal models should focus on the chloramines and their effects on health. (65 Refs)

54. SURFACE ACTIVE AGENTS AS TUMOR PROMOTERS (MEETING ABSTRACT).

Boyland E

London School of Hygiene and Tropical Medicine, London, England

International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Initiation and promotion are different stages in carcinogenesis. Initiators are generally mutagenic and if a substance or procedure is carcinogenic and not mutagenic the effect is most probably tumor promotion. Many carcinogens are complete, having both initiating and promoting activity. Promoters alone induce tumors because initiators are present in the diet or the environment. Promoters can be physical as with trauma and foreign bodies such as with asbestos. Promoters are often organotropic; phenobarbitone, clofibrate and valium act on the liver of rodents. Of the 14 types of tumor promoters listed, the class of surfactants includes many different compounds. Saccharin, cyclamate and tryptophan act on the rat bladder, and lithocholic acid on the colon. The sweetening agents and bile acids reduce interfacial tension by some 20% in concentrations at which they are present in urine or feces when given in doses which promote tumors in rats. The incidence of cancer of esophagus and mouth is high in smokers who consume spirits rather than beer. The cigarette provides initiators and the alcohol acts as promoter. The alcohol present in spirits would reduce the interfacial tension appreciably in the mouth and esophagus so that the carcinogenic action of spirits is probably due to the promoting action of the alcohol because of its surface activity. With promoters of the surfactant type there are levels below which the effects are negligible and so there may be safe levels. This is clearly the concentration attained at any particular time rather than the total dose. The effect of the surface active tumor promoters is probably due to action on cell membranes. The mode of action of solvents such as chloroform and benzene is probably similar. There must be safe or threshold levels for the surface active and other promoters, but probably not for materials like asbestos which remain in the body. It is possible that there are no safe levels for initiators, but if there were they might vary with exposure to promoters. (no Refs)

55. THE TWO-GENERATION SACCHARIN BIOASSAYS (MEETING ABSTRACT).

Arnold DL

Health Protection Branch, Ottawa, Canada

International Symposium on Health Effects of Tumor Promotion, October 12-15, 1981, Cincinnati, Ohio US Environmental Protection Agency and the American College of Toxicology; 1981

Saccharin was discovered over 100 yr ago and the controversy regarding its safety for human consumption started shortly therafter and has not subsided appreciably in the intervening decade. The consumption of saccharin, particulary in North America, started to escalate when under new standards of identity, the US Food and Drug Administration allowed foods containing artificial sweeteners to be promoted as 'nonnutritive' or 'noncaloric' sweeteners for use by the general public. In 1969, when cyclamates were banned, at least 10 single generation feeding studies were undertaken to more accurately assess the toxicological consequences resulting from the anticipated increased consumption of saccharin. While none of these studies resulted in any overt regulatory action, the introduction of the two-generation chronic toxicity/carcinogenicity bioassay added a new total to the toxicologists' arsenal. Three studies have since been conducted using the pro-

tocol. and the results from these studies clearly show that when rats were exposed to diets containing 5 or 7.5% sodium saccharin from the time of conception to death, and increased frequency of urinary bladder cancers were predominately found in the males. While some study results suggested that impurities in commercial saccharin, or the presence of urinary tract calculi may have been responsible for the observed bladder tumors, it now appears that these possibilities are highly unlikely. The mechanisms by which saccharin elicited the bladder tumors using the two-generation experimental model has not been ascertained. (no Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

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DIETARY FACTORS IN CARCINOGENESIS

1. NUTRITION AND ENVIRONMENTAL HEALTH: THE INFLUENCE OF NUTRITIONAL STATUS ON POLLUTANT TOXICITY AND CARCINOGENICITY. VOLUME 2: MINERALS AND MACRONUTRIENTS.

Calabrese EJ

Environmental Health Program, Div. Public Health, Univ. Massachusetts, Amherst, MA

Nutrition and Environmental Health: The Influence of Nutritional Status on Pollutant Toxicity and Carcinogenicity. Volume 2: Minerals and Macronutrients. New York, John Wiley and Sons, 468 pp., 1981.

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

2. RETROSPECT AND PROSPECT OF STUDIES ON DIGESTIVE SYSTEM DISEASES IN CHINA.

Zhang X

Dept. Internal Medicine, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China

Zhonghua Xiaohua Zazhi; 1(1):1-4 1981

In CHI

3. EPIDEMIOLOGY OF PITUITARY ADENOMAS.

Gold EB

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:163-183 1981

4. BLADDER CANCER EPIDEMIOLOGY.

Matanoski GM, Elliott EA

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 North Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:203-229 1981

5. THE EPIDEMIOLOGY OF BENIGN BREAST DISEASE.

Ernster VL

Dept. Epidemiology and International Health, 1699HSW, Univ. California, San Francisco, CA, 94143

Epidemiol Rev; 3:184-202 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

6. AIR POLLUTION AND BIOLOGICAL DEFENCE.

Schlipkoter HW, Dolgner R

Med. Institut fur Umwelthygiene an der Univ., Gurlittstrasse 53, D-4000 Dusseldorf 1, W. Germany

Zentralbl Bakteriol [Orig A]; 172(4/5):299-311 1981

In GER

7. CANCER AND THE PHYSICOCHEMICAL QUALITY OF DRINKING WATER IN QUEBEC.

Thouez JP, Beauchamp Y, Simard A

Dept. Geography, Univ. Montreal, Montreal, Quebec, Canada

Soc Sci Med [Med Geogr]; 15(1):213-223 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

8. ONCOGENIC VIRUSES.

Wyke JA

Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England

J Pathol; 135(1):39-85 1981

9. ROLE OF VIRUSES IN THE ETIOLOGY OF NATURALLY OCCURRING FELINE LEUKEMIA.

Essex M, Grant CK, Cotter SM, Hardy Jr WD

Dept. Microbiology, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA, 02115

Haematol Blood Transfus; 26:483-487 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

10. MAMMALIAN IN VIVO AND IN VITRO CYTOGENETIC ASAYS: A REPORT OF THE U.S. EPA'S GENE-TOX PROGRAM.

Preston RJ, Au W, Bender MA, Brewen JG, Carrano AV, Heddle JA, McFee AF, Wolff S, Wansom JS

Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830

Mutat Res; 87(2):143-188 1981

11. BACTERIAL SYSTEMS FOR CARCINOGENICITY TESTING.

Mohn GR

Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands

Mutat Res; 87(2):191-210 1981

12. MUTAGENESIS BY CHEMICAL AGENTS IN V79 CHINESE HAMSTER CELLS: A REVIEW AND ANALYSIS OF THE LITERATURE.

Bradley MO, Bhuyan B, Francis MC, Langenbach R, Peterson A, Huberman E

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Mutat Res; 87(2):81-142 1981

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13. CANCER BIOLOGY.

Ruddon RW

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Cancer Biology. New York, Oxford University Press, 344 pp., 1981

14. AVOIDABLE CANCER: ATTRIBUTION OF RISK.

Doll R

Radcliffe Infirmary, Oxford, England

S Afr Cancer Bull; 25(3):125-146 1981

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ORGAN SITE CARCINOGENESIS

Kidney and Urinary Tract

SERIES CK17 No. 82/05

MAY, 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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HE 20.3173/2:

PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. GEOGRAPHICAL DISTRIBUTIONS OF BALKAN ENDEMIC NEPHROPATHY AND OF NEOPLASMS OF THE KIDNEY PELVIS AND URETERS.

Nikolich I, Ostojic B
Urological Clinic, Medical Faculty, Belgrade, Yugoslavia
Urol Nefrol (Mosk); (5):20-24 1981

The incidences of Balkan endemic nephropathy (EN) and kidney pelvis and ureteral neoplasms (KPUN) were studied in the Lazarevac region of Yugoslavia. From 1952 to 1978, a total of 54 cases of KPUN were recorded in the region. Among these cases, 51 were diagnosed in villages with high incidences of EN. It was estimated that the risk of KPUN tumors in the villages with high incidence of EN was 93x greater than that in the villages free of EN. (12 Refs) (In RUS)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

2. EVIDENCE OF A MULTIPLICATIVE EFFECT BETWEEN CIGARETTE SMOKING AND OCCUPATIONAL EXPOSURES IN THE AETIOLOGY OF BLADDER CANCER.

Vineis P, Segnan N, Costa G, Terracini B
Servizio di Epidemiologia dei Tumori, Universita di Torino e Ospedale Maggiore, via Santena 7, 10126 Torino, Italy
Cancer Lett; 14(3):285-290 1981

Risk of bladder cancer resulting from the combined effects of exposure to tobacco smoke and occupational history was examined. Analysis of 225 case-control pairs (men, av age 59.0 yr for cases and 58.9 yr for controls) revealed an overall relative risk of developing bladder cancer of 4.8 for exposure to tobacco smoke and 1.7 for particular occupations (chemical industry, dye production, tire factories, petrol refining, gas plants, and typographers). The relative risk for smokers regardless of number of cigarettes smoked was 4.4 in non-occupationally exposed men, compared with 6.8 in occupationaly exposed men. The findings suggest a multiplicative effect between occupational exposure and cigarette smoke in human bladder carcinogenesis. (27 Refs)

3. EPIDEMIOLOGIC STUDY OF DRINKING WATER CHLORINATION AND WISCONSIN FEMALE CANCER MORTALITY.

Young TB, Kanarek MS, Tsiatis AA
Dept. Preventive Medicine, Univ. Wisconsin, 504 North Walnut St., Madison, WI, 53706
JNCI; 67(6):1191-1198 1981

The association between gastrointestinal, urinary tract, brain, lung, and breast cancer mortality and drinking water trihalomethane exposure, as estimated by av daily chlorine dosage of water source 20 yr past, was investigated for Wisconsin white females by use of a death certificate-based case-control study design. A total of 8,029 cancer deaths and 8,029 controls (non-cancer deaths) matched on county of residence, year of death, and age were taken from mortality records of 28 counties for the years 1972-77. Data on characteristics and treatment of municipal water supplied to the residences of cases and controls were obtained from questionnaires sent to the water superintendents of the 202 waterworks associated with the sample. By the use of logistic regression analysis, odds ratios for site-specific cancer death associated with high, medium, and low chlorine-dosed water as compared to unchlorinated water exposure were determined; the control variables were urbanicity, marital status, and occupation. With the exception of cancer of the colon, no anatomic cancer site was significantly associated with any chlorine dose exposure category. For colon cancer, odds ratios of 1.51 [95% confidence interval (CI) = 1.06-2.14], 1.53 (95% CI = 1.08-2.0) and 1.53 (95% CI = 1.11-2.11) were obtained for high-, medium-, and low-dose chlorin ation, respectively (p less than or equal to 0.02). For colon cancer cases and controls exposed to water sources affected by rural runoff, odds ratios of 3.30 (95% CI = 1.45-7.48), 3.60 (95% CI = 1.57-8.26), and 2.74 (95% CI = 1.10-6.88) were observed for high, medium, and low chlorine dosages 20 yr past (p less than 0.025). (Author abstract) (40 Refs)

4. EPIDEMIOLOGICAL STUDY OF WORKERS ENGAGED IN THE MANUFACTURE OF CHROMIUM COMPOUNDS.

Satoh K, Fukuda Y, Torii K, Eng M, Katsuno N
Nippon Chemical Industrial Co., Ltd., 9-15-1 Kameido, Koto-ku, Tokyo 136, Japan
JOM; 23(12):835-838 1981

This is a study of the mortality of individuals engaged in the manufacture of chromium compounds (chromium work) at a plant in Tokyo, Japan, for 1 or more yr. Morbidity data and results of liver and kidney function tests were also reviewed. The subjects of the mortality study were 896 males, who engaged in the chromium work between 1918 and 1975. Workers who died or retired or left the work for other reasons before the end of the follow-up period (1978) and for whom the necessary data were obtainable are included. When compared with Japanese males, this group of workers was found to have a standard mortality ratio for respiratory cancer of 9.2, which indicates an excess risk. No excess risk of death was indicated for cancer in other organs of the body or for other diseases. No significant differences in morbidity, which would indicate that the exposed group contracted any specific diseases, including liver and kidney disorders, more easily than did the control group, were found. (Author abstract) (11 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

5. RAMJET FUEL TOXICOLOGY.

Back KC
Toxic Hazards Div., Aerospace Medical Res. Lab., Wright-Patterson Air Force Base, OH
Sci Tech Aerosp Rep; 19(18):2532 1981

Fuels containing isomers of perhydromethylcyclopentadiene (RJ4), reduced dimers of bicyclohepadiene (RJ5), a tricyclodecane compound (JP10) and methylcyclohexane were studied for their acute, subacute, and chronic toxicity. The agents are of low order toxicity from acute exposure. Chronic toxicity studies were run on RJ4, and JP10 using rats, mice, dogs and monkeys. Kidney and liver hyperplasia in RJ4 exposed rats and pulmonary irritation in dogs and monkeys exposed to RJ4 and RJ5 emerge as the salient results. Although there is some indication of increased tumor incidence in a small number of mice

held for 1 yr after exposure to near saturated RJ5 vapors, there is no clear cut evidence that this compound is carcinogenic. (Author abstract) (no Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

6. MICROSOMAL NITROREDUCTASE ACTIVITY OF RABBIT KIDNEY AND BLADDER: IMPLICATIONS IN 5-NITROFURAN-INDUCED TOXICITY.

Zenser TV, Mattammal MB, Palmier MO, Davis BB
Geriatric Res., Educatgion and Clinical Center (111G JB), Veterans Admin. Medical Center, St. Louis, MO, 63125
J Pharmacol Exp Ther; 219(3):735-740 1981

The reductive microsomal metabolism of N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide and p-nitrobenzoic acid was studied in different areas of the rabbit kidney. In view of the relatively low oxygen tension in the renal inner medulla and bladder mucosa, the results suggest that medullary and transitional epithelial nitroreductases may be involved in the pathogenesis of 5-nitrofuran toxicity. (50 Refs)

7. ELEVATED LEVELS OF ORNITHINE DECARBOXYLASE AND POLYAMINES IN THE KIDNEYS OF ESTRADIOL-TREATED MALE HAMSTERS.

Nawata H, Yamamoto RS, Poirier LA
Nutrition and Metabolism Section, Lab. Carcinogen Metabolism, NCI, Bethesda, MD, 20205
Carcinogenesis; 2(11):1207-1211 1981

The effects of 17 beta-estradiol (E2) on the levels of ornithine decarboxylase (ODC), S-adenosylmethionine decarboxylase (SAMDC), and of the polyamines putrescine, spermidine and spermine in the kidneys of castrated male hamsters were determined. The ip injection of E2 into male hamsters led to renal ODC levels three times above the control levels 6-12 hr after treatment. Similarly, the renal ODC levels in hamsters treated with chronic doses of E2 for 60-180 days were 1.5-1.9 times the corresponding enzyme levels in control, sham-operated animals. With a series of estrogen analogues, there was a direct correlation between the rise in renal ODC in vivo and the binding to renal estradiol receptor sites in vitro. The hamster kidney levels of the polyamines putrescine, spermidine and spermine all declined during the 180-day experimental period. A single ip injection of E2 led to a 70% increase in renal SAMDC activity 12 hr after treatment. However, the administration of E2 for 180-270 days was without effect on the normal age-dependent decline in SAMDC levels noted in kidneys. These results indicate that, like other carcinogens and promoters, E2 increases the levels of ODC and of polyamines in its target tissue and that the rise in ODC is mediated by a specific estradiol-binding protein. (Author abstract) (30 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

8. HISTOCHEMICAL FINDINGS SUGGESTING THAT METHYLAZOXYMETHANOL, A LIVER AND KIDNEY CARCINOGEN, IS A SUBSTRATE FOR HEPATIC AND RENAL CHOLINE DEHYDROGENASE.

Tan QH, Penkovsky L, Zedeck MS
(c/o Zedeck) Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Carcinogenesis; 2(11):1135-1139 1981

The potent carcinogen, Methylazoxymethanol (MAM), induces tumors predominantly in rat liver, colon and kidney. The findings reported in this paper suggest that MAM is a substrate for the enzyme choline dehydrogenase located in rat hepatocytes and in the terminal portion of the rena l proximal convoluted tubule. As with the natural substrate choline, this reaction with MAM did not require NAD+, was not inhibited by pyrazole and was dependent on the electron transfer reagent, phenazine methosulfate. The product of this reaction is probably the same as that obtained from the metabolism of MAM by alcohol dehydrogenase, namely, an unstable aldehydic derivative which decomposes rapidly to carbonium ions. The reaction with alcohol dehydrogenase offered an explantation for the organotropic effects of this carcinogen in liver and colon and the current report provides a mechanism for the induction of kidney tumors as well as another possible means for production of liver tumors. (Author abstract) (16 Refs)

9. HISTOLOGICAL RENAL CHANGES AFTER SHORT-TERM PREOPERATIVE IRRADIATION. A CONTRIBUTION TO THE PATHOGENESIS OF IRRADIATION-INDUCED KIDNEY DAMAGE.

Theuring F, Roder K
Institut fur Pathologie, Radiologische Klinik der Medizinischen Akademie, Leipziger Strasse 44, DDR - 3010 Magdeburg, E. Germany
Zentralbl Allg Pathol; 125(4):346-353 1981

Early morphological changes caused by irradiation of the kidneys are presented. Due to hypernephroid carcinomas, the tumor-carrying renal ends were exposed to 1,100-3,150 rad during 2 wk and nephrectomy was performed 3-7 days later. At this time, changes of all renal structures were evidenced by light microscopy. Their irradiation specificity and reversibility or irreversibility are discussed. Very early and simultaneous lesions of the renal structures were essential findings in our material. In the sequel, secondary renal hypertonia and glomerular nephrosis additionally occurred. The human kidney was found to be an organ sensitive to radiation. This should be considered when applying irradiation to the renal region. (Author abstract) (15 Refs) (In GER)

10. LIGHT AND ELECTRON MICROSCOPIC FINDINGS IN PREOPERATIVELY IRRADIATED HUMAN RENAL CELL CARCINOMAS.

Fritzsche V, Katenkamp D, Unger G, Kob D
Pathologisches Institut, Friedrich-Schiller-Universitat, Ziegelmuhlenweg 1, DDR-6900 Jena, E. Germany
Zentralbl Allg Pathol; 125(4):354-363 1981

The study presents the light and electron microscopic changes in human renal cell carcinomas after preoperative irradiation. The findings of 6 irradiated renal cell carcinomas were

compared with those of 2 non-irradiated tumors. A total dose of 30 Gy was applied, given in 20 doses. The light microscopic and histochemical studies did not show a significant difference between irradiated and non-irradiated tumors. Electron microscopy revealed differences between irradiated and non-irradiated renal cell carcinomas. The mostly centrally localized nucleus of the tumor cells showed a nuclear edema, moderately to highly activated nucleoli and an increased amount of different types of nuclear bodies. The cytop lasm demonstrated a changing content of organelles, which predominantly consisted of mitochondria. Here and there sub-plasmalemmally localized intracytoplasmatic microfilaments were found. The stroma cells corresponded to mesenchymal or fibroblast-like cells and sometimes showed bundles of microfilaments, which were arranged parallel to the long axis of the cell. They produced morphological similarities to myofibroblasts. The capillaries were clearly activated, the basement membrane appeared multilayered and sometimes included compartments of ground substance. The intracellular space contained finely granulated material, typical collagen fibers and cross-banded structures with similarities to 'long-spacing' collagen. From the findings can be inferred that irradiation in therapeutic doses has a direct effect on tumor cells and an effect on vessels, which, above all, produces inflammatory reactions. (Author abstract) (28 Refs) (In GER)

11. MESOBLASTIC NEPHROMA: A MALIGNANT TUMOR WITH A LOW DEGREE OF MALIGNITY.

Willnow U

Klinik und Poliklinik fur Kinderchirurgie, Karl-Marx-Universitat, Bereich Medizin, Oststr. 21-25, DDR-7050 Leipzig, E. Germany

Z Urol Nephrol; 74(10):749-754 1981

A case history of mesoblastic nephroma (MN) occurring in a newborn infant is reported, and aspects of MN are reviewed. A palpable mass was detected in the left mid-abdominal region at birth. Infusion urography indicated an almost nonfunctional left kidney. During transabdominal surgery 20 days after birth, a tumor involving the medial and cranial lobes of the left kidney was found. No metastases were present. Ureteronephrectomy was performed. Three wk after surgery digestive disruption and vomiting occurred. Relaparotomy revealed severely necrotic enterocolitis. The infant died of sepsis nine days after relaparotomy. Histological examination of the tumor showed fiber-forming cells resembling fibroblasts or leiomyoblasts, as well as primitive glomeruli and undifferentiated tubules. Studies of the kinetics of tumor cells showed a 3H-thymidine marking index of 5.8%, DNA synthesis time of 18.2 hr, mean generation time of 141.1 hr, growth fraction of 0.28, and potential doubling time of 16.4 days, all indicative of a low grade of malignity. MN was thus distinct from rapidly growing, highly malignant Wilm's tumors. MN occurs almost exclusively in newborn and young infants. Prognosis after ureteronephrectomy is better the younger the infant is at treatment. (18 Refs) (In GER)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

12. NEW ANTIGEN INDUCED BY HERPES SIMPLEX VIRUS IN HUMAN TUMORS.

Posevaia TA, Kosiakova NP, Barinskii IF, Kosiakov PN, Pavliuchenkova RP

D. I. Ivanovskii Inst. Virology, Moscow, USSR

Vopr Virusol; (5):597-601 1981

Infection of biopsy specimens of various human tumors with herpes simplex virus was found to induce a new antigen not only in neoplasms of the uterus, cervix, and ovary but also in those of the kidney and bladder. The antigens induced in the cervical carcinoma had the highest complement-fixation activity. (13 Refs) (In RUS)

13. INTEGRATION OF FOREIGN GENOME FRAGMENTS INTO CELLS TRANSFORMED OR COTRANSFORMED WITH FRAGMENTED ADENOVIRAL DNA.

Tikchonenko TI, Chaplygina NM, Kalinina TI, Gartel AL, Ponomareva TI, Naroditsky BS, Dreizin RS

D. I. Ivanovsky Inst. Virology, Acad. Medical Sciences USSR, Moscow 123098, USSR

Gene; 15(4):349-359 1981

DNA integration of highly oncogenic simian adenovirus type 7 (SA7) and non-oncogenic human adenovirus type 6 (Ad6) into the genome of newborn rat kidney cells transformed by fragmented DNA preparations was studied. SA7 and Ad6 transformation, expression of integrated viral sequences, Ad6-pBR322 plasmid cointegration comprised the study. Intact DNA transformation, transformation by fragmented DNA, shortening of integrated DNA, and competence of eukaryotic cells are discussed. Reassociation kinetics and spot hybridization were employed. DNA was fragmented with the specific endonucleases SalI and endonuclease BglII. Cells transformation by fragmented DNA resulted in integration of the left-hand fragment and other regions of the viral genome with the oncogene. Integrated fragments were stable during numerous passages of cell lines. In the case of the Ad6-transformed cell line integrated fragments were not expressed. Mass losses of 25-50% occurred with the integration of SA7 DNA fragments. The linear form of pBR322 plasmid contributed to the Ad6 DNA integration into the genome of the transformed cell. (40 Refs)

14. STUDY OF THE IMMUNITY MEDIATED BY CELLS IN 291 PATIENTS WITH MALIGNANT GENITOURINARY TUMORS.

Glait HM, Scorticati C, Feierstein JN, Bellora O, Koss A, Olivari AJ

Centro Oncologico de Medicina Nuclear, Instituto de Oncologia 'Angel H. Roffo', Buenos Aires, Argentina

Radiodiagn Radioter; 1(2):51-73 1981

Immunological states of 291 patients (14-88 yr old) with malignant genitourinary tumors (MGUT) were evaluated. Changes in the MGUT patients after hormonal treatment and radiotherapy were analyzed and were compared with changes in 27 patients that had benign urinary disease (BUD). The locations of the tumors were as follows: bladder (99), prostate (80), testicle (55), penis (20), kidney (28), and multiple (9). The following immunologic tests were performed: 2,4-dinitrochlorobenzene (DNCB), Candida antigen (CA), streptokinase-streptodornase (SK/SD), phytohemagglutinin (PHA), alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA),

and circulating immune complexes (CIC). Every 3 mo different follow-up tests were performed depending on the location of the disease. The results for the BUD patients were as follows: DNCB (25 ug) positive (pos) in 48.1%, DNCB (100 ug) pos in 85.2%, CA pos in 48%, SK/SD pos in 59.3%, and blastic transformation normal in 68.4%. These results were lower than those for normal healthy persons. The results for the malignant tumor patients were presented according to location of tumor, stage of tumor, clinical evolution, use of radiotherapy, use of hormonal treatment, and histology (only in the cases of testicular seminoma). Correlation was observed between immunologic state and the evolution of the disease; this was most clearly demonstrated in non-patients with seminoma malignant tumors of the testicle, for whom the evolution of the disease and early diagnosis of relapse or metastases could be monitored. (36 Refs) (In SPA)

REVIEWS AND OTHER RELATED STUDIES

15. OCCUPATIONALLY RELATED CARCINOGENESIS.

Waite DE
Dept. Family Medicine, Fee Hall, Michigan State Univ., East Lansing, MI, 48824
JAOA; 80(5):350-355 1981

The epidemiology of industrial carcinogenesis is discussed. The association between cancers of the urinary bladder and occupational exposure to workers in the German coal tar industry was first made in 1895 by Rehn. Cancer of the nose associated with chromate production was reported in 1890, and lung cancer from the same exposure in 1912. During the 1940s and 1950s the marked expansion of industry led to a significant increase in the number of observed relationships between occupational exposure and subsequent development of cancer. The Occupational Safety and Health Administration (OSHA), established in 1970, determines standards for exposure to carcinogens in industrial operations. OSHA currently exercises stringent controls over 19 specific chemicals which it labels as 'cancer specific agents.' Mechanisms of chemical carcinogenesis, primary carcinogens, and secondary carcinogens are also discussed. (42 Refs)

16. CANCER CYTOGENETICS: A RE-EVALUATION OF ITS SIGNIFICANCE.

Hsu TC
Dept. Cell Biology, Univ. Texas, M. D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030
Med Pediatr Oncol; 9(5):524-525 1981

Cytogenetics of familial and nonfamilial human cancers and of cancers in experimental animals are described. Specific chromosomal aberrations have been associated with human cancers including retinoblastoma, Wilm's tumor, and renal cell carcinoma. Chromosomal changes in medullary thyroid neoplasia and Gardner's syndrome have been reported. Nonrandom chromosomal alterations have been observed in murine T-cell leukemia and in neurogenic tumors induced in rats. Chromosomal aberrations have been noted in various human leukemias and lymphomas. (no Refs)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. CHEMICAL CARCINOGENESIS.
Farber E
Dept. Pathology, Univ. Toronto, 100 College St., Toronto, ON M5G 1L5, Canada
N Engl J Med; 305(23):1379-1389 1981

2. N-HEXANE AND ITS TOXICOLOGIC EFFECTS. A REVIEW.
Jorgensen NK, Cohr KH
Harevaenget 44, DK-4200 Slagelse, Denmark
Scand J Work Environ Health; 7(3):157-168 1981

3. SAFROLE: ITS METABOLISM CARCINOGENICITY AND INTERACTIONS WITH CYTOCHROME P-450.
Ioannides C, Delaforge M, Parke DV
Dept. Biochemistry, Univ. Surrey, Guildford, Surrey GU2 5XH, England
Food Cosmet Toxicol; 19(5):657-666 1981

RADIATION CARCINOGENESIS

4. CARCINOGENIC, MUTAGENIC, TERATOGENIC WORKSHOP.
Suit H, Hall E, Frei E
Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114
Cancer Clin Trials; 4(Suppl):37-41 1981

5. DOSIMETRY OF THE ATOMIC BOMB SURVIVORS.
Sinclair WK, Failla P, Bond VP, Loewe WE, Kerr GD, Auxier J, Wyckoff OH, Maruyama T, Schull JW, Land EC, Dobson LR, Mays WC, Seymour J
Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439
Radiat Res; 88(3):437-447 1981

DIETARY FACTORS IN CARCINOGENESIS

6. NUTRITION AND CANCER: A REVIEW.
Muller E, Rickenbach M
Institut fur Sozial- und Praventivmedizin, Universitat Zurich, Gloriastrasse 32 B, 8006 Zurich, Switzerland
Praxis; 70(43):1903-1912 1981
In GER

7. FLAVONOIDS, MUTAGENS, AND CITRUS.
Horowitz RM
U. S. Dept. Agriculture, Agricultural Res. Service, Fruit and Vegetable Chemistry Lab., Pasadena, CA, 91106
ACS Symp Ser; 170:43-59 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

8. ETIOLOGICAL CONCEPTS IN CERVICAL CARCINOGENESIS.
Kessler II
Dept. Epidemiology and Preventive Medicine, Univ. Maryland Sch. Medicine, 655 West Baltimore St., Baltimore, MD, 21201
Gynecol Oncol; 12(2,part2):S7-S24 1981

9. CURRENT CONCEPTS ON THE AETIOPATHOGENESIS OF ACUTE LEUKAEMIA.
Torres A, Martinez Guibelalde F, Gomez Garcia P, Garcia Castellano JM, Manzanares Escribano MR
Jefe Servicio Hematologia, Ciudad Sanitaria 'Reina Sofia' de la Seguridad Social, Cordoba, Spain
Sangre (Barc); 26(5B):700-717 1981
In SPA

10. CANCER FAMILY SYNDROME.
Svendsen LB, Bulow S
Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
Ugeskr Laeger; 143(42):2713-2716 1981
In DAN

11. GENETIC AND BIOCHEMICAL STUDIES WITH ATAXIA TELANGIECTASIA.
Huang PC, Sheridan RB
Dept. Biochemistry, Sch. Hygiene and Public Health, Johns Hopkins Univ., Baltimore, MD, 21205
Hum Genet; 59(1):1-9 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

12. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.
Kalmaz EV, Kalmaz GD
Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916
Chemosphere; 10(10):1163-1175 1981

13. CHEMICAL AND ENVIRONMENTAL AGENTS IN GASTROINTESTINAL CARCINOGENESIS.
Deschner EE, De Cosse JJ, Sherlock P
Lab. Digestive Tract Carcinogenesis, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Clin Gastroenterol; 10(3):755-771 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

14. THE REPAIR OF DNA DAMAGE: RECENT DEVELOPMENTS AND NEW INSIGHTS.
Friedberg EC, Bonura T, Love JD, McMillan S, Radany EH, Schultz RA
Dept. Pathology, Lab. Experimental Oncology, Stanford Univ., Stanford, CA, 94305
J Supramol Struct Cell Biochem; 16(1):91-103 1981

MODIFICATION OF CARCINOGENESIS

15. ROLE OF HORMONES INCLUDING DIETHYLSTILBESTROL (DES) IN THE PATHOGENESIS OF CERVICAL AND VAGINAL INTRAEPITHELIAL NEOPLASIA.
Robboy SJ, Truslow GY, Anton J, Richart RM
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Gynecol Oncol; 12(2,part2):S98-S110 1981

16. PROSTAGLANDINS AND CANCER: A REVIEW OF TUMOR INITIATION THROUGH TUMOR METASTASIS.
Honn KV, Bockman RS, Marnett LJ
Dept. Biological Sciences, Wayne State Univ., Detroit, MI, 48202
Prostaglandins; 21(5):833-864 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

17. GENITAL CANCER AND VIRUSES.
Rapp F, Jenkins FJ
Dept. Microbiology, Pennsylvania State Univ. Coll. Medicine, Hershey, PA, 17033
Gynecol Oncol; 12(2,part2):S25-S41 1981

18. VIRUS PAPILLOMAS IN HUMANS.
Nasemann T
Univ.-Hautklinik Eppendorf, Martinistr. 52, D-2000 Hamburg 20, W. Germany
Hautarzt; 32(11):601-606 1981
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. A THORACIC BENIGN MESENCHYMOMA IN ASSOCIATION WITH HEMIHYPERTROPHY.

Majeski JA, Paxton ES, Wirman JA, Schreiber JT
Dept. Surgery, Medical Univ. South Carolina, Charleston, SC, 29425
Am J Clin Pathol; 76(6):827-832 1981

A thoracic benign mesenchymoma was removed from an 18-yr-old caucasian male who also had hemihypertrophy. The very large benign mesenchymoma which was removed was found to consist of an admixture of cytologically mature vascular spaces, adipose tissue, and smooth muscle. After removal of the tumor, the patient has had no recurrence with 1 yr of follow-up. Patients with hemihypertrophy appear to be at a high risk to develop neoplasms. Malignant neoplasms of the adrenal gland, kidney, and liver are most common. It is suggested that patients with hemihypertrophy should be followed periodically for their entire life because of their propensity to develop tumors. (Author abstract) (15 Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

2. ABUSE OF PHENACETIN-CONTAINING ANALGESICS AND CARCINOMA OF THE RENAL PELVIS.

Syre G, Matejka M
Pathologisch-Anatomisches Institut, Universitat Wien, Spitalgasse 4, A-1090 Wien, Austria
Wien Klin Wochenschr; 93(13):420-423 1981

A retrospective analysis of 39 carcinomas of the renal pelvis that had been treated between 1968-1979 revealed capillary sclerosis in 12 cases. In 18 patients no capillary sclerosis was seen, and 9 tumors could not be analyzed. Since in 25% of the cases with capillary sclerosis phenacetin abuse was known, the sale of that analgesic should be professionally controlled. Patients, who receive phenacetin regularly, should be submitted to regular cytologic examination. Moreover, the obligation of the physician to inform the patient about the advantages and disadvantages of a treatment should include the cancer risk in case of phenacetin treatment. (27 Refs) (In GER)

3. THE CONTRIBUTION OF CANCER REGISTRIES IN VICTORIA AND NSW TO CANCER PREVENTION AND CONTROL (MEETING ABSTRACT).

Ford J, Dodds A
No affiliation given
Clinical Oncology Society of Australia, November 24-27, 1981, Melbourne, Australia. The Society 70 pp., 1981.

Since 1940, the Central Cancer Registry of Victoria has collected data on a number of variables from public cancer patients attending 10 contributing hospitals in the metropolitan area of Melbourne. The Registry has had an 'end results' and 'treatment intention' orientation but is expanding to universal registration. An assessment of cancer incidence is possible for particular sites, as for most cancers the Registry covers about half of the possible cases: relative frequencies of cancer by site are estimated. Time trends in the ratio of early to late stages at time of diagnosis and the length and quality of survival in relation to particular sites by stage and treatment are discussed. The Central Cancer Registry of NSW is a population-based Registry established in 1972. Descriptive data have been published for all sites for 1972 to 1977 and show geographical variations with other countries: Migrant patterns with statistically significant differences when compared with Australian born, eg high stomach cancer in Greek and British males and females, low colon cancer in Southern Europeans, time trends in female lung cancer with a significant rise 1972 to 1977. A case-control study has shown a ten-fold relative risk of renal p elvis cancer in females with regular analgesic consumption, and an increased risk ratio in males. (no Refs)

4. COFFEE DRINKING AND CANCER OF THE LOWER URINARY TRACT.

Morrison AS, Buring JE, Verhoek WG, Aoki K, Leck I, Ohno Y, Obata K
Dept. Epidemiology, Harvard Univ. Sch. of Public Health, 677 Huntington Ave, Boston, MA, 02115
JNCI; 68(1):91-94 1982

The relation of coffee drinking to the incidence rate of cancer of the lower urinary tract ('bladder cancer') was evaluated. Broadly based series of cases and series of controls drawn from the general population of each area were assembled and interviewed in Boston, Massachusetts (587 cases, 528 controls), Manchester, England (541 cases, 725 controls), and Nagoya, Japan (289 cases, 586 controls). Compared to drinkers of an average of less than one cup of coffee per day, those who drank more had a relative risk of bladder cancer estimated as 1.0 (0.8-1.2, 95% confidence interval). With adjustment for cigarette smoking habits, only small and irregular changes in risk were seen with increasing frequency of coffee consumption. Duration of coffee drinking showed little relation to risk of bladder cancer. Apparent associations of coffee drinking and bladder cancer may be due to incomplete control of the effect of cigarette smoking. If there is a true association of coffee drinking and bladder cancer, it is likely to be weak. (Author abstract) (12 Refs)

5. OCCUPATIONAL BLADDER CANCER AND CIGARETTE SMOKING IN WEST YORKSHIRE.

Glashan RW, Cartwright RA
(c/o Cartwright) Yorkshire Regional Cancer Organisation, Cookridge Hosp., Leeds LS16 6OB, England
Br J Urol; 53(6):602-604 1981

This paper reports the preliminary findings of a case-controlled study of bladder cancer in parts of West Yorkshire. The first 991 cases have been analyzed, and the results of the occupational exposure for five occupations are reported. There is an increased risk of bladder cancer associated with smoking cigarettes in both males and females. These results take both the age and the year of diagnosis into account and are statistically significant. Chemical industry workers and printers have been shown statistically to have a high risk ratio, whereas leather workers, hairdressers and dye-users have a statistically insignificant risk ratio. For process workers in the dye manufacturing industry, the length of service is significantly correlated with the risk of bladder cancer; so is the age at which a man first becomes a process worker. (Author abstract) (12 Refs)

6. THE EARLY CHANGES IN THE DEVELOPMENT OF BLADDER CANCER IN PATIENTS EXPOSED TO KNOWN INDUSTRIAL CARCINOGENS.

Glashan RW, Wijesinghe DP, Riley A
Dept. Urology, Huddersfield Royal Infirmary, Lindley, Huddersfield, Yorkshire, England
Br J Urol; 53(6):571-577 1981

In the Huddersfield district many people have been exposed to industrial carcinogens as a result of their occupation. An exfoliative urine cytology screening program has been in operation for many years so that patients with the early changes associated with these carcinogens are referred for urological investigation at a very early stage in the disease. A description of the development of urothelial dysplasia, carcinoma in situ and transitional cell carcinoma is presented, with particular reference to the urine cytology, histological features of mucosal biopsies and cystoscopic appearances of the bladder. Changes in the collagen fibers in the basement membrane are also described. (Author abstract) (8 Refs)

7. ARTIFICIAL SWEETENERS IN RELATION TO THE EPIDEMIOLOGY OF BLADDER CANCER.

Howe GR, Burch JD
NCI Canada Epidemiology Unit, Univ. Toronto, Ontario, Canada
Nutr Cancer; 2(4):213-216 1981

Three types of studies of the possible association between artificial sweeteners and cancer are reviewed; temporal trend studies, studies of diabetics, and case-control studies. Animal studies have provided strong evidence for the carcinogenicity of saccharin. The methodological problems need further investigation. Avoidance of the use of artificial sweeteners is advised. (23 Refs)

8. MULTIPLE MALIGNANCY WITH A FAMILIAL TENDENCY.

Forrest J, Slaney G, Crocker J, Hallam J, Taylor AM
Dept. Surgery, Univ. Birmingham, Birmingham, England
Clin Oncol; 7(4):357-364 1981

The patient described died in 1980 from a carcinoma of the lung which was his ninth primary malignancy. Previous cancers had arisen in the skin, cecum, ileum, kidney, bladder, rectosigmoid colon, descending colon and stomach. All these tumors with the exception of the bladder were treated by surgical resections over a 16 yr period and at autopsy no evidence of recurrence of any of them was evident. One other 'tumor' also reported as a carcinoma and arising in the patient's larynx proved on review to have controversial histological features and is therefore not included. The male line of this man's family had a very high cancer record, and three members of two generations have died in their fourth and fifth decades with bowel cancer. Other benign lesions treated surgically included Crohn's ileitis and prostatic hyperplasia. Cellular studies failed to reveal anything exceptional in the response of his cultured cells to three different types of DNA damaging agent (x-rays, UV light or mitomycin C). (Author abstract) (3 Refs)

9. EPITHELIAL LESIONS OF BLADDER MUCOSA FOLLOWING URETERAL REIMPLANTATION.

Kroovand RL, Chang CH, Broecker BH, Perrin EV, Oldford J, Perlmutter AD
Dept. Pediatric Urology, Children's Hosp. Michigan, Detroit, MI
J Urol; 126(6):822-823 1981

We report on three children who underwent ureteral reimplantation. Postoperative ly, each patient had persistent, irritative, lower urinary tract symptoms and continuous or recurring urinary infections, with or without gross hematuria. Because of these symptoms cystoscopy was done in two children and the third child underwent repeat ureteral reimplantation because of persistent vesicoureteral reflux. At operation single or multiple hyperplastic, sessile lesions of the urothelium, not evident at the time of initial ureteral reimplantation, were discovered in each child. Histologically, these lesions showed proliferative and metaplastic glandular epithelial changes. Treatment consisted of transurethral fulguration and long-term antimicrobial medication plus partial cystectomy and topical intravesical chemotherapy for recurrent lesions in 1 child. The etiology of these epithelial lesions, although uncertain, is believed to be response to long-standing inflammation. (Author abstract) (12 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

10. MAMMARY CARCINOMA INDUCED BY ORAL ADMINISTRATION OF ETHYL METHANESULPHONATE. DETERMINATION OF SOME OF THE PARAMETERS AFFECTING TUMOR INDUCTION.

Ueo H, Takaki R, Yamagami H, Sugimachi K
Johns Hopkins Univ., Sch. Hygiene and Public Health, 615 North Wolfe St., Baltimore, MD, 21205
Carcinogenesis; 2(12):1223-1228 1981

The carcinogenic activity of ethyl methanesulfonate (EMS), an alkylating agent and a potent mutagen, was examined in Wistar King A and Sprague Dawley rats following oral administration. In the Wistar King A rats, mammary carcinomas were detected in all of the young female rats by the 32nd wk after initiation of the experiment. To determine the optimal experimental conditions for the rapid and invariable induction of mammary carcinomas, the relationship among age, sex, strain of the rats and concentration and duration of EMS administration, and tumor production was investigated. The tumor incidence was higher in the younger female rats and the Wistar rats were more susceptible than Sprague-Dawley rats. Mammary carcinomas were also induced in the younger male rats. In addition, concomitant production of renal tumors occurred by the 40th wk in young rats administered 10(-2) M or 2 x 10(-2) M of EMS soln, while renal and uterine tumors developed concomitantly in the older female rats given 3 x 10(-3) EMS by the 56th wk. Histologically, the prevailing features of tumors were infiltrating ductal adenocarcinoma in the mammary glands, mesenchymal tumor in the kidney, and leiomyosarcoma in the uterus. Methyl methanesulfonate, an analogue of EMS, did not induce tumors in any organs. (Author abstract) (7 Refs)

11. CARCINOGENICITY EXAMINATION OF INFLORESCENCE OF ZINGIBER MIOGA ROSCOE (MEETING ABSTRACT).

Mori H, Kato K, Hirono I, Hosaka S, Aiso S
Department of Pathology, Gifu University, Gifu, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The carcinogenicity of mioga was examined in ACI and Fisher 344 rats. In Experiment I, a test group of ACI rats re-

ceived a diet containing mioga (1 part of mioga to 2 parts of basal diet) for 365 days. The experiment was terminated 480 days after the start of feeding. In Experiment II, a test group of Fisher 344 rats received the diet of mioga throughout the experiment of 639 days. Female ACI rats in Experiment I developed significantly more urinary bladder tumors than the control group. No carcinogenic activity was observed in males in Experiment I or males and females in Experiment II. Recently, the presence of L-arginine in a methanol extract of mioga and induction of bladder carcinomas in mice with implanted pellets containing L-arginine are reported. In this study, carcinogenicity of L-arginine and possible promoting effect on bladder carcinogenesis with N-Butyl-N-(4-hydroxy butyl)nitrosamine were also examined in ACI and Fisher rats by oral administration of 0.5% L-arginine soln. However neither carcinogenicity nor promoting effect was detected in both strains. (no Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

12. EFFECT OF PHENOBARBITAL, POLYCHLORINATED BIPHENYL AND SODIUM SACCHARIN ON HEPATIC AND RENAL CARCINOGENESIS IN UNILATERALLY NEPHRECTOMIZED RATS GIVEN N-ETHYL-N-HYDROXYETHYLNITROSAMINE ORALLY.

Hirose M, Shirai T, Tsuda H, Fukushima S, Ogiso T, Ito N
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
Carcinogenesis; 2(12):1299-1302 1981

The effects of phenobarbital (PB), polychlorinated biphenyl (PCB) and sodium saccharin (SS) on hepatic and renal carcinogenesis induced by N-ethyl-N-hydroxyethylnitrosamine (EHEN) were examined in male F344 rats. The rats were given 0.1% EHEN in their drinking water for 2 wk and then diet containing 0.05% PB, 0.05% PCB or 5% SS for 32 wk. In wk 3, the right kidney was removed to promote renal neoplasia. The incidence of hepatocellular carcinoma was much higher in rats given PB or PCB than in controls given EHEN alone. PB administration significantly decreased the av number of renal-cell tumors per unit area and SS reduced the numbers of early neoplastic nodules. Treatment with PCB had no effect on renal carcinogenesis. These results indicate that chemicals may have either a promotive or inhibitory effect depending on the organ. (Author abstract) (25 Refs)

13. ENHANCING EFFECT OF URINE ON BLADDER CARCINOGENESIS BY MNU (MEETING ABSTRACT).

Miyata Y, Babaya K, Oyasu R
Department of Pathology, Northwestern University Medical School, Chicago, IL
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 198 1, Sapporo, Japan. The Association 415 pp., 1981.

It has been firmly established that urine plays an important role in urinary bladder carcinogenesis. Using a heterotopically transplanted rat bladder (HTB), we have demonstrated that normal urine has a tumor enhancing effect on bladder carcinogenesis. In that study, however, the bladder epithelium was exposed to carcinogen in the presence of urine, and possible involvement of urine in the initiation step could not be ruled out. The present investigation was conducted with 2 major goals in mind: 1) to remove the possible effect of urine during the initiation step, and 2) to establish a model system where potential modifiers of bladder carcinogenesis may be tested. Young male Fisher rats, 4 wk post transplant, were divided into 6 groups. For the first 2 groups, 0.25 mg of methyl-1-nitrosourea (MNU) was instilled directly into HTB once a wk 3 x. A wk after the last dose, one half of rats received normal rat urine into HTB (group 1), and the other half 0.9% saline (group 2) weekly. The second 2 groups of rats received a single dose of MNU, and subsequently urine (group 3) or saline (group 4). Groups 5 and 6 rats served respectively as urine and saline controls without prior exposure to carcinogen. The bladder cancer incidences in HTB's are as follows: group 1, 16/18; group 2, 6/18; group 3, 14/23; group 4, 2/22; group 5, 1/19; and group 6, 0/18. The results indicate urine plays an enhancing role in the bladder where epithelial cells initiated by carcinogen in the urine-free environment. The schedules established above may be useful to test the role of modifiers of carcinogenesis. (1 Ref)

14. DEHYDROEPIANDROSTERONE: AN ANTI-OBESITY AND ANTI-CARCINOGENIC AGENT.

Schwartz AG, Hard GC, Pashko LL, Abou-Gharbia M, Swern D
Fels Res. Inst., Temple Univ., Philadelphia, PA, 19140
Nutr Cancer; 3(1):46-53 1981

Effects of long-term administration of dehydroepiandrosterone (DHEA) on female C3H-Avy/A (obese) and C3H-A/A (non-obese) mice were examined. DHEA treatment significantly inhibited wt gain in both strains of mice without suppressing food consumption. Food consumption of the DHEA-treated C3H-A/A mice was significantly greater than that of controls. DHEA significantly reduced the rate of breast cancer development. From 12 to 18 mo of age, the difference in breast cancer rates between controls and DHEA-treated C3H-A/A mice was significant. In the C3H-Avy/A mice, significant differences in breast cancer rates between controls and DHEA-treated mice were evident between 10 and 15 mo. The C3H-Avy/A control mice experienced a marked enhancement in rate of breast cancer development when compared to the C3H-A/A control group. A single ip injection of DHEA (15 mg/kg) inhibited 12-O-tetradecanoylphorbol-13-acetate (TPA) stimulation of 3H-thymidine incorporation in mouse epidermis. DHEA also blocked the TPA stimulation of 3H-th ymidine incorporation in a rat kidney epithelial cell line; the inhibition was reversed by culturing for 20 hr in medium without DHEA. The results suggest that DHEA has an anti-carcinogenic effect and may have pharmacologic value in cancer prevention. (29 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

15. ARYLAMIDASES FROM HUMAN HEPATIC AND RENAL CANCER TISSUES IN COMPARISON WITH NORMAL TISSUE ENZYME (MEETING ABSTRACT).

Sumikawa K, Yamamoto H, Hada T, Higashino K
Third Department of Internal Medicine, Osaka University School of Medicine, Osaka, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Arylamidases were solubilized from human hepatic and renal cancer tissues by bromelain treatment, and their properties were compared with the normal tissue enzymes. An electro-

phoretic study showed that the most rapidly migrating activity was that of the normal liver enzyme, and that the most slowly migrating activity was that of the normal kidney one. The hepatic and renal cancer tissue enzymes yielded activity with intermediate mobility. However, the enyzmes from four sources were indistinguishable with respect to the other physicochemical and immunological properties. These results may suggest that these four enzymes were synzymes which were coded by the identical structure gene. (no Refs)

16. GAMMA-GLUTAMYL TRANSPEPTIDASE IN A NEWLY ESTABLISHED CELL LINE FROM HUMAN RENAL CARCINOMA, OUR-10.

Hada T, Higashino K, Yamamoto H, Okochi T, Sumikawa K, Watanabe S, Matsuda M, Osafune M, Kotake T, Sonoda T
Third Dept. Internal Medicine, Osaka Univ. Medical Sch., Fukushima 1-1-50, Fukushima-ku, Osaka 553, Japan
Gan; 72(6):842-847 1981

A newly established cell line, OUR-10, from human renal carcinoma seems to have the same gamma-glutamyl transpeptidase as the novel one which was found recently in renal carcinoma tissue; the enzymic properties such as electrophoretic mobility, Km value, mol wt, thermostability, the effects of urea, sodium dodecyl sulfate and sulfhydryl reagents, the effects of amino acids, cations and EDTA, and the binding behavior to a concanavalin A-Sepharose column were the same as those of the novel gamma-glutamyl transpeptidase found in renal carcinoma tissue. The immunological properties of the gamma-glutamyl transpeptidase (GGTP) of OUR-10 examined by inhibition tests and tests of cross-reactivity with anti-normal kidney GGTP antibody were also the same as those of the novel gamma-glutamyl transpeptidase. These results may mean that the novel gamma-glutamyl transpeptidase originates from the cancer cells, and can be used as a marker for identification of this cell line, OUR-10. (Author abstract) (19 Refs)

17. SPECIFIC BINDING OF THE TUMOR PROMOTER TPA IN VARIOUS MOUSE ORGANS AS MEASURED B Y A 'COLD ACETONE-FILTER ASSAY'.

Hergenhahn M, Hecker E
Inst. Biochemistry, German Cancer Res. Center, D-6900 Heidelberg, W. Germany
Carcinogenesis; 2(12):1277-1281 1981

Rapid, specific, saturable and partially reversible binding of the tumor promoter 12-O-tetradecanoylphorbol-13-acetate ([3H]TPA) to a particulate fraction of mouse brain can be demonstrated by means of a 'cold acetone-filter assay'; by washing with cold acetone at-20 C, nonspecific binding of the highly lipophilic [3H]TPA to membranes can be reduced to approx 10% of the total binding. A comparative study of homogenates of several organs with this test revealed specific [3H]TPA binding/ug DNA in the order; brain is much greater than lung, which is approx = spleen, which is approx = liver, which is approx = kidney, which is approx = thymus, which is approx = ovaries. Specific binding sites were also detected in 600 x g supernatant fractions of homogenates from epidermis, forestomach, glandular stomach and small intestine. Competition experiments showed displacement of [3H]TPA by TPA greater than phorbol-12,13-didecanoate greater than 12-deoxyphorbol-13-tetradecanoate greater than phorbol-12,13-dibutyrate (PDBu) greater than phorbol-12,13-diacetate greater than 4-O-methyl-TPA greater than 4alpha-phorbol-12,13-didecanoate in the brain particulate fraction. Specific [3H]TPA binding is sensitive to heat, periodate and dithiothreitol, but is relatively insensitive to urea or to 1-5% soln of several common detergents. It is estimated that the present binding test is approx 500x more sensitive than the widely-accepted [3H]PDBu assay; perhaps more important, the present method employs TPA, which is extremely effective both as a tumor promoter in vivo and as a pleiotropic effector of cells in vivo and in vitro. (Author abstract) (18 Refs)

18. METABOLISM AND BINDING OF BENZO(A)PYRENE AND 2-ACETYLAMINOFLUORENE BY SHORT-TERM ORGAN CULTURES OF HUMAN AND RAT BLADDER.

Moore BP, Hicks RM, Knowles MA, Redgrave S
Sch. Pathology, Middlesex Hosp. Medical Sch., Riding House St., London W1P 7LD, England
Cancer Res; 42(2):642-648 1982

The ability of organ cultures of normal human and rat bladder to metabolize the polycyclic hydrocarbon, benzo(a)pyrene (BP), and the arylamine, 2-acetylaminofluorene, has been studied. Cultures were maintained for 0 to 6 days in a chemically defined medium before incubation with [3H]BP (0.3 to 0.5 uM) or 2-[14C]acetylaminofluorene (18 to 25 uM) for 24 hr. Ethyl acetate-soluble and water-soluble metabolites were produced from both compounds by both species. The ethyl acetate extracts from [3H]BP-treated human cultures contained 9,10-dihydro-9,10-dihydroxybenzo(a)pyrene, 7,8-dihydro-7,8-dihydroxybenzo(a)pyrene, and 3-hydroxybenzo(a)pyrene. Rat bladder cultures produced similar metabolites but i n slightly different proportions. Ethyl acetate-soluble products of 2-[14C]acetylaminofluorene from human cultures contained 7-hydroxy-2-acetylaminofluorine, 9-hydroxy-2-acetylaminofluorene, 2-aminofluorene, and N-hydroxy-2-acetylaminofluorene. Rat bladder cultures produced similar metabolites, but 2-aminofluorene was found in relatively higher proportion. Hydrolysis by beta-glucuronidase of the water-soluble products produced from both carcinogens gave ethyl acetate-extractable derivatives. These hydrolyzable glucuronide conjugates were relatively more abundant following metabolism of the carcinogens by the rat than by the human cultures. Covalent binding to DNA occurred with [3H]BP in both human (19.7 +-13 pmol/mg DNA) and rat cultures (22.8 +-8.6 pmol/mg DNA). As with other human tissues, considerable variation (50-fold) was observed between individuals. The results demonstrate that both human and rat bladder epithelium can metabolize known potent carcinogens and, in the case of BP, can effect covalent binding between the products of metabolism and the urothelial cell DNA. In theory, carcinogenesis in the urinary bladder could thus be initiated by carcinogens produced or excreted in the urine without the necessity for their prior metabolism elsewhere in the body. (Author abstract) (66 Refs)

19. URINARY METABOLITES OF 3,3'-DICHLOROBENZIDINE AND THEIR MUTAGENICITY.

Tanaka KI
Toray Shiga Hosp., 7-35, Sonoyama 2-chome, Otsu 520, Japan
Sangyo Igaku; 23(4):426-427 1981

3,3'-dichlorobenzidine (DCBZ) was administered to rats, urinary metabolites of the DCBZ, 3,3'-dichloro-N-acetylbenzidine (N-AcDCBZ) and 3,3'-dichloro-N,N'-diacetylbenzidine (NN'-AcDCBZ), were observed in the urine of the rats, and mutagenicity of the DCBZ, N-AcDCBZ, and NN'-AcDCBZ was investigated using Salmonella typhimurium TA 98 and TA 100 and a revertant mutagenicity test. Spectrographic pure DCBZ was administered po (20 mg) to five rats (Group 1), per trachea (10 mg) to five (Group 2), and pc (200 mg) to five (Group 3); five rats were not administered the DCBZ. DCBZ,

N-AcDCBZ, and NN'-AcDCBZ were detected with both gas chromatography and high pressure liquid chromatography in the urine of Group 1 and 2 rats. Only NN'-AcDNBZ was observed in the urine of Group 3 rats. With the aid of Ames test, mutagenic activity of 1 ml urine samples containing N-acetyl DCBZ metabolites was shown to increase with the concentration of the metabolites in the urine samples from the Group 1 and 2 rats, but no mutagenic activity was observed for the 1 ml samples from the Group 3 rats. The mutagenic activity of the NN'-AcDCBZ was much lower than that of the DCBZ or the N-AcDCBZ. These techniques were thought to be applicable for study of mechanisms of carcinogenicity of these metabolites as well as for biological monitoring of the substances. (7 Refs) (In JPN)

20. METABOLIC FATE OF ASYMMETRIC N,N-DIALKYLNITROSAMINES HAVING A BUTYL GROUP IN THE RAT.

Suzuki E, Okada M
Tokyo Biochemical Res. Inst., Takada 3-14-8, Toshima-ku, Tokyo 171, Japan
Gan; 72(6):910-920 1981

The metabolic fate of N-alkyl-N-butylnitrosamines (alkyl = ethyl, propyl, and pentyl), which induce tumors in the liver and esophagus but do not induce bladder tumors, was investigated in the rat, in order to elucidate any possible correlation between metabolism and the noncarcinogenicity to the urinary bladder of these N-nitrosamines. They were extensively metabolized in the rat, no unchanged compounds being found in the urine. The metabolic pattern of these N-nitrosamines having a butyl chain was essentially similar to that of N,N-dibutylnitrosamine, which induces tumors in the bladder as well as in the liver and esophagus. They were mainly metabolized via omega-oxidation followed by beta-oxidation and/or (omega-1)-oxidation of either of the two alkyl chains. Thus the N-alkyl-N-(3-carboxypropyl)nitrosamine and/or the N-alkyl-N-(2-carboxyethyl)nitrosamine were identified as the principal urinary metabolites. Possible important factors concerned with the induction of bladder tumors by N,N-dialkylnitrosamines are discussed from the metabolic point of view. (Author abstract) (21 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

21. COMPARATIVE INVESTIGATIONS ON PROLIFERATION KINETICS, CELL SURFACE RECEPTORS, AND HISTOLOGY IN RENAL CELL CARCINOMA (MEETING ABSTRACT).

Klein HO, Dias Wickramanayake P, Klein PJ, Vierbuchen MJ, Ortmann M, Lehmann HD
Medical Clinic, University Cologne, Cologne, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

There are only few reports on biological characteristics of hypernephroma. In 64 cases we tried to determine by means of flow-, single cell cytophotometry, in vitro autoradiography (double labeling), analysis of cell surface receptors (lectins +/- neuraminidase pretreatment) and histology as well as case history whether there is a correlation between these parameters and prognosis. Specimen were investigated 10-15 min post operation. They were excised from the marginal and central area of the tumor. The DNA distribution displayed predominantly in 32% a diploid, in 6.890% a hypodiploid, in 13.690% a hyperdiploid, and in 47.7% a heterogeneous tumor population with polyploidic stem lines. The labeling index of tumor cells varied between 5 and 15%. The duration of S-phase was between 10-20 hr. The tumors exhibited a wide range of the quantity and distribution of cell surface receptors (lectin binding sites). Treatment with neuraminidase increased the number of receptor sites in 61% of the cases. Results concerning the correlation of these findings will be presented. (no Refs)

22. CYTOPHOTOMETRIC STUDY OF HUMAN CANCERS OF THE LUNG, LARYNX, AND KIDNEY AND WILMS' TUMOR TRANSPLANTED INTO ATHYMIC MICE. COMMUNICATION III.

Revazova ES, Petrova AS, Zubrikhina GN, Iudicheva TV
All-Union Cancer Res. Center, Moscow, USSR
Lab Delo; (12):726-728 1981

Ploidies of human kidney cancer (KC), Wilms' tumor (WT), laryngeal cancer (LAC), and lung cancer (LC) were studied following transplantation of the tumors into athymic nude mice. Cytophotometric analysis showed that 73.7% of the cells in the KC had diploid DNA contents. Triploid cells comprised 30-35% of the proliferative pools of the WT, LAC, and LC. The cells with tetraploid DNA contents comprised 25.1% of the proliferative pool of the LC, compared with 20.1% in the WT and 11.9% in the LAC. (2 Refs) (In RUS)

23. CANCERS OF THE KIDNEY IN 1981.

von Niederhausern W
Departement d'urologie, CHUV, 1011 Lausanne, Switzerland
Rev Med Suisse Romande; 101(10):777-782 1981

The histopathology, diagnosis, and treatment of renal neoplasms (RN) are discussed. Adenocarcinomas, characterized by clear cells, account for 80-85% of RN and most often occur in 40-70 yr old men. Transitional cell carcinoma (9% of cases), squamous cell carcinoma (1%), sarcomas (2-3%) may occur in the kidney. Wilms' tumor, which occurs in children less than 6 yr old, accounts for 20-25% of cancer cases in young children. The TNM classification of RN is presented. At the time of diagnosis, 40% of RN are Stage I, 15% Stage II, 25% Stage III, and 20% Stage IV. The differential diagnosis of RN and renal cysts is discussed. The diagnostic importance of the presence or absence of painful hematuria is considered. Technics important in the diagnosis of RN or monitoring the development of RN include cystoscopy, iv urography, needle biopsy, arteriography, cavography, computed transverse tomography, and exfoliative cytology. Symptoms related to the prognosis of RN are reported. Nephrectomy is the most common treatment for RN. Other treatments useful in the management of RN include renal artery embolization, specific or non-specific immunotherapy, chemotherapy, hormone therapy, and preoperative radiotherapy. The management of pulmonary metastases in RN patients is considered. (no Refs) (In FRE)

24. ESTABLISHMENT AND CHARACTERIZATION OF A CELL LINE (SS78) FROM A HUMAN RENAL CELL CARCINOMA.

Shrivastav S, Sharief Y, Day J, Reich CF, Bonar RA
Duke Univ. Medical Center, Box 3813, Durham, NC, 27710
In Vitro; 17(12):1117-1124 1981

A new cell line, SS78, was established from a primary renal cell carcinoma of a Caucasian male. The tissue was dispersed with collagenase, and viable cells were separated by flotation on a Ficoll-Hypaque gradient. In culture, the SS78 cells retained a distinct epithelial morphology, and no fibrob lastlike cells were seen. The cultured cells were aneuploid with a modal chromosome number of 80 and had several marker chromosomes. Inoculation of the cultured cells into athymic nude mice caused tumors at the sites of inoculation. (Author abstract) (32 Refs)

25. CARCINOMA OF THE RENAL PELVIS AND URETER.

Stambolis C, Doppl W, Pust R, Hocke M, Kracht J
Zentrum fur Pathologie der Univ., Langhansstrasse 10, D-6300 Giessen, W. Germany
Med Welt; 32(49):1859-1865 1981

Carcinoma of the renal pelvis and ureter (CRPU) is reviewed. Two cases involving the renal pelvis, ureter and bladder are reported. Both cases were treated by ureteronephrectomy. Primary epithelial neoplasms account for 96.4% of the upper urinary tract, of which 3/4 are malignant. Solitary papillomas of the renal pelvis develop in 25 % of CRPU cases; multiple papillomas develop in 50% of cases. Risk factors for CRPU include inflammation, urinary stones, urothelial metaplasia, the use of Thorotrast in pyelography, and occupational exposure to aniline derivatives. CRPU are less frequent than renal cell or bladder carcinomas. CRPU occur most frequently in the 6th-8th decades of life. Unifocal tumors occur predominantly in the caudal third of the kidney. Lymphatic metastases may develop in the paraaortic, paracaval, iliac, and paravesicular nodes. Clinical signs and symptoms include hematuria, flank pain, and urinary obstruction. Histological types include transitional cell (91-92%) and squamous cell (8%) carcinoma, adenocarcinoma (less than 1%), and undifferentiated carcinoma (less than 1%). Diagnostic and differential diagnostic techniques include excretion urography, retrograde pyelogram, cystoscopy, ultrasonography, renal angiography, and surgical biopsy. Prognosis depends on histologic type, manner of infiltration, degree of anaplasia, and stage. Principal treatment is ureteronephrectomy with excision of a wedge of bladder tissue. (24 Refs) (In GER)

26. CORRELATION OF CYTOLOGY WITH HISTOPATHOLOGY AND CYSTOSCOPY IN URINARY BLADDER TUMOURS.

Javali D, Singh SM, Gupta NP, Wadhwa SN
Dept. Urology, All India Inst. Medical Sciences, New Delhi 110 029, India
Indian J Cancer; 18(4):241-244 1981

Cytologic results are correlated with cystoscopic and histopathologic findings in 114 cases of urinary bladder tumor. A total of 93 cases had transitional cell carcinoma. Urinary cytology was less precise in cases of lower grade tumor. The remaining 21 cases showed squamous cell carcinoma, rhabdomyosarcoma, adenocarcinoma and undifferentiated type. Cystoscopic examination of 112/114 cases revealed tumor or tumors. Positive results in cytology increased with tumor multiplicity. There were two false positive cytologic cases. Thus cytology was positive in 69/114 cases. As tumor size increased, so did the success rate of cytology. In 22 cases, urinary cytology reports were negative, and in 23 were inconclusive. Most of these consisted of low grade tumors. Urinary cytology was found to be a very useful tool in the diagnosis and follow-up of bladder tumors. (21 Refs)

27. THE PROGNOSTIC MEANING OF MARKER CHROMOSOMES IN HUMAN URINARY BLADDER CARCINOMA (MEETING ABSTRACT).

Harbott J, Burk K
Urol. University Klinik, 3550 Marburg/Lahn, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

Prognostic statements of later infiltration concerning human urinary bladder cancer cannot be given by histological and cytological investigations. Cytogenetic analyses indicate a relationship between chromosomal abnormalities and infiltration of the tumor. Tumor tissue is brought to colchicine soln immediately after transurethral resection without any culturing. The cells then are treated with a hypotonic soln, fixed, and spread in acetic acid. The slides are air dried and strained in Giemsa soln. By karyotyping ploidy and marker chromosomes are registered. In the investigated tissues different marker chromosomes were found, some of which were very similar. In the recurrences of a tumor the same marker chromosomes reappear. Number and characteristics of marker chromosomes were brought in relation to histological data. Whereas marker chromosomes were found in all carcinoma of the stages T2 and T3, they appear only in one third of the noninvasive tumors. These results correspond to the fact, that approx 30% of the superficial urinary bladder carcinoma become invasive. By karyotyping potential invasive tumors may be recognized in a preinvasive stage, which indicates an aggressive therapy. (no Refs)

28. COMBINED CELL SURFACE ANTIGENS AND CHROMOSOMAL STUDIES IN BLADDER CANCER.

Javadpour N, Roy JB, Bottomley R, Dagg K
Surgery Branch, NCI, Bethesda, MD, 20205
Urology; 19(1):29-32 1982

The conventional histopathologic examination of a primary tumor does not predict the potentiality for invasiveness and recurrence of a superficial low-grade transitional cell carcinoma of the bladder. We have utilized combined cell surface antigens and chromosomal analysis to predict the natural history of the bladder cancer in 20 patients in a double blind study. In this preliminary report it appears that both cell surface antigens and chromosomal abnormalities correlate well with the stages and grades of bladder cancer. (Author abstract) (12 Refs)

29. CELL CYCLE KINETICS OF REGENERATING UROTHELIAL CELLS OF THE RAT URINARY BLADDER AFTER PARTIAL CYSTECTOMY.

Kunze E, Woltjen HH, Nehm FJ, Schauer A
Center Pathology, Univ. Gottingen, Robert-Koch-Str. 40, D-3400 Gottingen, W. Germany
Virchows Arch [Cell Pathol]; 38(1):117-125 1981

The cell cycle kinetics of bladder urothelial cells regenerating after partial cystectomy were investigated in 96 female Wistar rats using the percentage labeled mitoses method. In the area of resection a mean cell cycle time (TC) of 15 hr was determined. The DNA synthesis phase (TS) lasted 6 hr and the

premitotic-postsynthetic phase together with the mitosis phase (TG2 + M) 1.5 hr, thus giving a presynthetic-postmitotic phase (TG1) of 7.5 hr. Similar values were found for the urothelial cells in the stump: the mean cycle time measured 14 hr, the TS-phase 6 hr, the TG2 + M-phase 2 hr and the TG1-phase 6 hr. These data are discussed with respect to known cell cycle parameters of bladder urothelium regenerating in response to cytotoxic agents and of neoplastic urothelial cells. The reported findings provide a basis for further investigations using weak carcinogens and threshold doses of potent carcinogens to test the working hypothesis that stimulation of proliferation following partial cystectomy is capable of initiating, accelerating and/or potentiating carcinogenic cell transformation in the urinary bladder. (Author abstract) (28 Refs)

30. EXTRACELLULAR MATRIX PROTEINS IN HUMAN BLADDER TUMORS (MEETING ABSTRACT).

Sakashita S, Hashi H
Department of Urology, Asahikawa Medical College, Asahikawa, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Fibronectin is a major component of non collagenous glycoproteins in extracellular matrix. Laminin is a relatively new glycoprotein localized in basement membrane. These proteins play a role in cell-cell contacts. We will show the difference of extracellular matrices between normal and malignant bladder tissues. Fibronectin was purified from human plasma by Gelatin-Sepharose. Laminin was purified as a previous report in ABB, 1980. By immunofluorescent technique, laminin was seen in basement membranes both of malignant and normal bladder. But fibronectin was lacking in the cell surface of malignant epithelium. The fact may be the rationale to explain the looseness of cell-cell adhesion in malignant cells as a cause of metastasis. (no Refs)

31. AN AUTOPSY CASE OF HORMONE-PRODUCING TRANSITIONAL CELL CARCINOMA OF URINARY BLADDER (MEETING ABSTRACT).

Kohga S, Hayashi T, Sumiyoshi A
Department of Pathology, Miyazaki Medical College, Miyazaki, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Hormone-producing transitional cell carcinoma of urinary bladder has not been reported. An autopsy case of this tumor is demonstrated. A 54-yr-old man with 1-yr history of macrohematuria was admitted to the hospital because of dry cough and high fever. On admission, gynecomastia was found and a bladder tumor was observed cytoscopically. Interesting laboratory findings were abnormal levels of hormones: Serum human chorionic gonadotropin (hCG) was 220120 mIU/ml, luteinizing hormone (LH) 500 mIU/ml, estron 1103 pg/ml, estradiol 452 pg/ml, plasma ACTH 400 pg/ml and cortisol 242 ng/ml. At autopsy, widespread metastases were found in the lungs and other groups. The tumor was a transitional cell carcinoma intermingled with giant cells including trophoblastic cells. Immunohistochemically, hCG was revealed in these tumor cells. (no Refs)

32. HEMATURIA AND BLADDER CANCER.

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Rev Med Suisse Romande; 101(10):771-776 1981

The diagnosis, (based on the presence of hematuria), treatment, and prognosis of bladder cancer (BC) are discussed. Ureteral hemorrhage unrelated to urination is most often caused by ureteral lesions. Hematuria at the beginning of urination is often (80% of the cases) indicative of a prostatic tumors. Hematuria at the end of urination may be related to urogenital tuberculosis, hemorrhagic cystitis, endometriosis, and bilharzia. BC may be indicated by any form of hematuria but is most often associated with complete hematuria with terminal exacerbation. In view of the poor prognosis associated with more advanced BC, patients with hematuria should undergo cystoscopy and urography. Histopathologically, BC may be classified as T1 (benign papilloma), T2 (non-infiltrating, submucosal, transitional cell carcinoma), T3 (infiltrating carcinoma), T4 (carcinoma with local and distant metastases). The treatment of BC is determined by tumor characteristics: histopathology, location, multiplicity, and degree of infiltration. Because T3 and T4 BC are usually associated with a poor prognosis, treatment should include both surgery and radiotherapy. Because radiotherapy produces 50% of secondary complications, surgery alone is recommended for patients with T1 and T2 BC. Other treatments for BC, such as brachytherapy, local thiotepa administration, and vitamin A, are described. Transureteral resection and other surgical technics involved in the treatment of BC are described. (no Refs) (In FRE)

33. GROWTH CHARACTERISTICS OF N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]-FORMAMIDE (FANFT)-INDUCED MOUSE BLADDER TUMOR LINES IN A HUMAN TUMOR STEM CELL ASSAY.

Niell HB, Mickey DD, Soloway MS, Wood CA
Hematology/Oncology Section, Veterans Admin. Medical Center, Coleman Res. Building, 956 Court, Memphis, TN, 38163
Cancer; 49(2):323-330 1982

Four N-[4-(5-nitro-2-furyl)-2-thiazolyl]-Formamide (FANFT)-induced mouse bladder tumor (MBT) lines were tested for their ability to form colonies in a tumor stem cell assay. Anticancer drug testing was done using this assay to determine whether reproducible colony survival curves could be pro duced. All four cell lines produced colonies at 10-14 days, whether taken from culture or murine tumor. Cloning efficiencies ranged from 0.29% to 1.93% from culture and from 0.005% to 0.05% from the murine source. Growth characteristics were described. Cells from colonies were histologically similar to the original cells plated. A linear relationship existed between the number of cells plated and the number of colonies produced. In vitro drug studies were reproducible and correlated with in vivo data. Therefore, MBT lines can be used for in vitro drug testing in a tumor stem cell assay and may be useful in selecting active chemotherapeutic agents in the murine tumor model. (Author abstract) (20 Refs)

34. CLEAR CELL ADENOCARCINOMA OF THE FEMALE URETHRA: CLINICAL AND ULTRASTRUCTURAL STUDY SUGGESTING A UNIQUE NEOPLASM.

Tanabe ET, Mazur MT, Schaeffer AJ
(c/o Mazur) Dept Pathology, Jewish Hosp. St. Louis, 216 S. Kingshighway, P.O. Box 14109, St. Louis, MO, 63178
Cancer; 49(2):372-378 1982

A case of clear cell adenocarcinoma arising in the female urethra is described. The tumor had a tubulocystic pattern and intracytoplasmic glycogen, resembling clear cell carcinomas that occur in the vagina and upper female genital tract. Ultrastructural study, however, showed abundant and elongated microvilli on the tumor cells, a feature not seen in clear cell carcinomas or other common forms of carcinoma arising in the

female genital tract. Six other cases of similar tumors of the female urethra were found in medical literature, yet there was no example of this tumor in the bladder or male urethra. Clinical and ultrastructural observations suggest that clear cell carcinoma of the female urethra is a distinctive neoplasm. Abundant microvilli provide morphologic evidence supporting the possibility of origin from the mesonephros. Radical extirpative surgery with urinary diversion appears to be the treatment of choice. (Author abstract) (31 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

35. NEW GLYCOPROTEIN ANTIGEN COMMON TO TERATOCARCINOMA, EMBRYONIC VISCERAL ENDODERM AND RENAL BRUSH BORDER (MEETING ABSTRACT).

Ozawa M, Yonezawa S, Sato E, Muramatsu T
Department of Biochemistry, Kagoshima University, Kagoshima, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

An antiserum was obtained by immunizing rabbits with glycoproteins isolated from murine teratocarcinoma OTT 6050 by affinity chromatography on Dolichos biflorus agglutinin-agarose. The antiserum, after absorption with sheep RBC and particulate fraction from liver of adult mice recognized a new glycoprotein antigen with restricted distribution. The antigen was detected on teratocarcinoma OTT 6050, visceral endodermal cells of 7-day-old mouse embryos and renal brush border, but not on a variety of tissues of other organs. In teratocarcinoma cultured in vitro, the antigen was intensively expressed on embryonal carcinomas cells apparently in the process of differentiation to endodermal cells. (no Refs)

36. ISOANTIGENS A,B,H IN BLADDER TUMORS AS AN INDICATOR OF MALIGNANT POTENTIAL: II SCANNING IMMUNOELECTRON MICROSCOPIC STUDY (MEETING ABSTRACT).

Kaneshige T, Kumon H, Ashai T, Matsumura Y, Ohmori H
Department of Urology, Okayama University, Okayama, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

The blood group ABO isoantigens (IA) have been shown to be present on the normal urothelium using the specific red cell adherence test. We reported previously that a progressive loss of IA on bladder tumor cells was associated with an increased malignant potential of bladder tumors. In this communication, the surface morphology and the distribution of IA on bladder tumors have been studied by scanning immunoelectron microscopy using bacteriophage T4 (T4) as a marker. Based on the surface features, pleomorphism of microvilli and the degree of attachment to the surrounding cells, tumor cells were classified into 5 main scanning electron microscopy (SEM) cell types. These SEM cell types correlated with not only the histological grade but also the degree of the deletion of IA expression. The characteristics of each cell type were discussed. We also examined bladder washing specimens from patients with or without bladder tumors. The presence or loss of IA on exfoliated urothelial cells could be detected clearly by T4-marker. The usefulness of this new cytological technique was also discussed. (no Refs)

37. THE CLINICAL SIGNIFICANCE OF TISSUE POLYPEPTIDE ANTIGEN (TPA) IN THE URINE OF BLADDER CANCER PATIENTS.

Kumar S, Costello CB, Glashan RW, Bjorklund B
Paediatric Oncology Lab., Christie Hosp. and Holt Radium Inst., Manchester M20 9BX, England
Br J Urol; 53(6):578-581 1981

A 2-stage study has been carried out to evaluate the usefulness of urinary tissue polypeptide antigen (TPA) levels in patients with bladder cancer as an adjunct to the routine procedures for detection of bladder tumors. Two-hr urine samples were collected from 83 bladder cancer patients and normal individuals for the first part of the study, 24-hr samples from 54 patients and normal individuals for the second part. Urinary TPA was determined using radioimmunoassay. In 2-hr samples there was no significant difference in the amounts of TPA/I in any of the groups. In contrast, the TPA results of 24-hr urine samples ($n = 54$) were markedly different from 2-hr samples, and the former correlated very well with the presence or absence of bladder cancer. A reason for this difference may be circadian rhythm effects. (Author abstract) (15 Refs)

38. SPONTANEOUS CELL-MEDIATED CYTOTOXICITY IN PATIENTS WITH TRANSITIONAL CELL CARCINOMA OF THE URINARY BLADDER. DIFFERENCE IN EFFECTOR CELL POPULATION.

Moroz C, Lindner A, Twig S, Madgar I, Many M
Rogoff-Wellcome Medical Res. Inst., Beilinson Medical Center, Petah-Tikva, Israel
Cancer Immunol Immunother; 12(1):57-62 1981

Spontaneous lymphocyte-mediated cytotoxicity (SLMC) of peripheral blood lymphocytes (PBL) from patients (male, av age 71) with transitional cell carcinoma (TCC) of the urinary bladder was studied. SLMC of PBL against K-562 cells varied greatly, but PBL from controls and patients did not differ in cytoxic activity over a range of effector:target ratios. Following separation of effector cells into T and non-T fractions, SLMC of T lymphocytes derived from TCC patients was significantly greater than that of non-T cell populations. In controls, cytotoxic activity of non-T cells was higher than that of T cells. Repeated experiments on two TCC patients over a 1 yr period consistently showed the high SLMC of T lymphocytes. The relatively higher SLMC of T cells from TCC patients was even more profoundly exhibited when Peer cells instead of K-562 cells were targets. Neither treatment with monoclonal antibodies OKT 8 or OKT 4 and complement nor use of preparations depleted of Fc-receptor-positive cells could abolish the cytotoxicity of T cells from cancer patients. The natural killer-like T cells are thought to be a disease-related phenomenon, but their nature remains unclear. (35 Refs)

39. TRANSFORMATION OF HAMSTER KIDNEY CELLS BY FRAGMENTS OF BK VIRUS DNA.

Grossi MP, Corallini A, Valieri A, Balboni PG, Poli F, Caputo A, Milanesi G, Barbanti-Brodano G
(c/o Barbanti-Brodano) Inst. Microbiology, Univ. Ferrara, 44100 Ferrara, Italy
J Virol; 41(1):319-325 1982

Hamster kidney cells were transformed, with comparable efficiency, by circular or linear molecules of complete BK virus (BKV) genome and by agarose gel-purified fragments of BKV DNA obtained by single or double digestions with various restriction endonucleases. Only fragments containing the complete early region of BKV DNA displayed transforming activi-

ty. Analysis by blot hybridization of the arrangement of viral DNA sequences in a cloned cell line transformed by a 3.8-kilobase fragment, obtained after sequential digestion of BKV DNA with HhaI and BamHI, showed the presence of seven viral integrations into the cellular DNA. Apparently all of the integrated viral molecules contained the entire early region of BKV DNA. Large T antigen, small t antigen, and the 56,000-dalton nonviral Tau antigen were detected in transformed cells by immunoprecipitation. The pattern of integration of viral sequences in transforme d cells was constant over many generations. Likewise, large T antigen was always detected in transformed cells at various passage levels. These results may suggest that all of the sequences of the early region coding for large T antigen are required for transformation by BKV. Alternatively, subgenomic segments of the BKV DNA early region may be unable to transform because the appropriate polyadenylation site, necessary to obtain a complete functional transcriptional unit, is removed by the restriction enzyme cleavage. (Author abstract) (34 Refs)

REVIEWS AND OTHER RELATED STUDIES

40. THE CHLORINATION QUESTION: HIGHLIGHTS OF THE RECENT CONFERENCE IN CALIFORNIA.

Hileman B
No affiliation given
Environ Sci Technol; 16(1):15A-18A 1982

Health problems associated with water chlorination, including alternative water disinfectants, epidemiological and carcinogenicity studies, cost benefit analysis, the chemistry of chlorination, and effects on aquatic ecosystems are discussed. Alternative disinfectants include chlorine dioxide (ClO2), ozone, and chloramines. ClO2 forms few chlorinated products. One disadvantage is production of the toxic chlorite ion which may possess antithyroid activity. Chloramines are thought to be mutagenic; ozone is expensive and short lived in water systems. Toxicological effects of chlorine have not been carefully studied, even though chlorine byproducts such as trihalomethanes, chlorinated phenols, and haloacetonitriles are possible carcinogens or mutagens. One study suggests a causal relationship between chlorinated drinking water and rectal, bladder, and colon cancer. A new method for measurement of residual halogens, which can detect less than 1 ppb, will allow closer monitoring of water supplies. Organic materials in natural waters are responsible for most of the observed reactions of chlorine with surface waters. Widespread use of chlorine as a water and food disinfectant warrants continued research into its beneficial and harmful effects. (no Refs)

41. AN EPIDEMIOLOGICAL BASIS FOR CANCER CONTROL.

Armstrong B
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Cancer Forum; 5(3):136-143 1981

Primary and secondary prevention of cancer, particularly cancer of the lung, breast, and colon and melanoma, which together account for greater than 40% of new cancer cases and premature mortality is discussed. Primary prevention aims at preventing cancer from occuring by ending exposure to the causal agent either by environmental or life type control. Lung cancer is attributable mainly to cigarette smoking; some cases result from occupational exposure. Breast cancer is associated with nulliparity, first full-term pregnancy at a comparatively late age, low parity, diet, radiation, post-menopausal estrogens , and oral contraceptives. Colon and rectal cancer are mainly related to dietary fiber deficiency and excess fat and meat consumption. Melanoma of the skin is due to exposure to UV radiation. Etiologies of other neoplasms are discussed: brain neoplasms (phenobarbitone use), prostate cancer (diet, cadmium exposure), stomach cancer (diet), leukemia (x-rays, benzene exposure, antineoplastic agent use), pancreatic cancer (diet, cigarette smoking), bladder cancer (occupational exposure to aromatic amines, cigarette smoking), and cervix cancer (sexual promiscuity). Dietary modification, cessation of smoking, and avoidance of excessive exposure to UV light was recommended. Screening methods involved in the secondary prevention of cancer include cervical cytology, proctosigmoidoscopy, and mammography at regular intervals for certain segments of the population. The choice between primary and secondary prevention of cancer is discussed. (20 Refs)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. ETHYLENE OXIDE (ETO): EVIDENCE OF CARCINOGENICITY.
Coene RF
National Inst. for Occupational Safety and Health, Cincinnati, OH
Vet Hum Toxicol; 23(6):439-443 1981

DIETARY FACTORS IN CARCINOGENESIS

2. NUTRITIONAL ASPECTS OF CANCER PREVENTION: AN OVERVIEW.
Silverman J
American Health Foundation, Naylor Dana Inst Disease Prevention, Valhalla, NY, 10595
J Am Vet Med Assoc; 179(12):1404-1409 1981

3. FORMATION OF N-NITROSO COMPOUNDS IN FOODS.
Gray JI
Dept. Food Science and Human Nutrition, Michigan State Univ., East Lansing, MI, 48824
ACS Symp Ser; 174():165-180 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

4. LYMPHOMAS AND LEUKAEMIAS. PART 2: TROPICAL AMERICA.
Jimenez E
Hospital Nacional de Ninos 'Dr. Carlos Saenz Herrera', Apartado 1654, San Jose, Costa Rica
Clin Haematol; 10(3):894-915 1981

5. LYMPHOMAS AND LEUKAEMIAS. PART 1: TROPICAL AFRICA.
Olweny CL
Uganda Cancer Inst., P.O. Box 3935, Kampala, Uganda
Clin Haematol; 10(3):873-893 1981

6. MALIGNANT MELANOMA.
Creagan ET
Div. Medical Oncology, Mayo Clinic, Rochester, MN, 55905
Compr Ther; 7(12):36-44 1981

7. MELANOTIC TUMORS OF THE UVEA AND RETINA.
Schmitt H
Universitats-Augenklinik, Theodor-Stern-Kai 7, D-6000 Frankfurt am Main, W. Germany
Med Klin; 76(24):672-675 1981
In GER

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

8. THE NATURAL HISTORY OF CARCINOGENESIS: IMPLICATIONS OF EXPERIMENTAL CARCINOGENESIS IN THE GENESIS OF HUMAN CANCER.
Pitot HC, Goldsworthy T, Moran S
McArdle Lab. for Cancer Res., Dept. Oncology, Medical Sch., Univ. Wisconsin, Madison, WI, 53706
J Supramol Struct Cell Biochem; 17(2):133-146 1981

9. CURRENT CONCEPTS AND CONTROVERSIES IN CHEMICAL CARCINOGENESIS.
Weinstein IB
Div. Environmental Sciences, Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Supramol Struct Cell Biochem; 17(2):99-120 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

10. BURKITT'S LYMPHOMA.
Ambrus JL, Ambrus CM
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Med; 12(6):385-413 1981

11. PRIMARY HEPATIC CARCINOMA.
Iosquin CJ
Catedra de Medicina Interna A, Facultad de Ciencas Medicas, La Plata, Argentina
Rev Fac Cienc Med La Plata; 4(2):27-31 1981
In SPA

METHODOLOGY IN CARCINOGENESIS RESEARCH

12. MUTAGENESIS AND CARCINOGENESIS TESTING IN VITRO.
Casto BC
Northrop Services, Incorporated, P.O. Box 12313, Research Triangle Park, NC, 27709
Biotechnol Bioeng; 23(12):2659-2671 1981

OTHER REVIEWS IN CARCINOGENESIS

13. CANCER IN THE YEAR 2000. A REVIEW.
Saxen E
Suomen Syoparekisteri, Liisankatu 21 B, 00170 Helsinki 17, Finland
Duodecim; 97(20):1708-1716 1981
In FIN

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ORGAN SITE CARCINOGENESIS

Kidney and Urinary Tract

SERIES CK17 No. 82/07 JULY, 1982

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. CANCER INCIDENCE AND MORTALITY IN METROPOLITAN NEW ORLEANS, 1974-77.

Halperin ST, Weilbaecher RG, Correa P, Krementz ET
Louisiana Tumor Registry, 2-3-4 Loyola Building, Suite 1000, New Orleans, LA, 70112
Natl Cancer Inst Monogr; 57:409-487 1981

Cancer incidence and mortality in metropolitan New Orleans (1974-77) is discussed in terms of primary site, race, sex, and age. Both malignant tumors and in situ lesions are considered. Ne w Orleans data show an overall high cancer incidence in blacks, mainly due to excessive rates for cancer of the lung, buccal cavity, esophagus, stomach, cervix, and prostate gland. For some cancers, including breast, ovary, bladder, and kidney cancers and the lymphoma-leukemia group, whites have a moderately excessive rate compared with blacks. Differences between New Orleans data and those obtained by the Surveillance, Epidemiology, and End Results Program are described. Particularly marked is the excess of respiratory cancer in New Orleans. (no Refs)

2. CANCER INCIDENCE AND MORTALITY IN PUERTO RICO, 1973-77.

Martinez I
Dept. Health, Cancer Control Program, Box 9342, Santurce, Puerto Rico, 00908
Natl Cancer Inst Monogr; 57:947-977 1981

Data on cancer incidence and mortality in Puerto Rico (1973-77) are presented by primary site and sex. Both malignant and in situ lesions are considered. Puerto Rico had a higher incidence of cancer of the mouth, hypopharynx, esophagus, stomach, and penis in comparison with findings for all Surveillance, Epidemiology, and End Results (SEER) Program areas. The incidence for all SEER areas, excluding Puerto Rico, was higher for cancers of the lip, colon, rectum, retroperitoneum, lung, bronchus, pleura, melanoma of skin, breast, corpus uteri, ovary, testis, urinary bladder, kidney, brain, endocrine glands, and lymphomas and leukemias. (no Refs)

3. CANCER INCIDENCE AND MORTALITY IN UTAH, 1973-77.

Lyon JL
Utah Cancer Registry, 540 Arapeen Drive, Room 204, Salt Lake City, UT, 84143
Natl Cancer Inst Monogr; 57:597-627 1981

Data on cancer incidence and mortality in Utah (1973-77) by age, sex, race, and primary site are presented. Both carcinomas and in situ lesions are considered. Utah has the lowest overall incidence of cancer for any of the Surveillance, Epidemiology, and End Results Program registries. The lower-than-expected incidence of cancer is attributed almost exclusively to the portion of the Utah population which is Mormon. Deficits noted for various cancer sites are heavily concentrated in those sites of the body associated with tobacco and/or alcohol use including the tongue, oral cavity, pharynx, larynx, esophagus, and urinary bladder. (no Refs)

4. CANCER MORBIDITY IN USSR IN 1979 (ANALYSIS OF MORBIDITY INDICES).

Napalkov NP, Merabishvili VM, Tserkovnyi GF, Preobrazhenskaia MN
No affiliation given
Vopr Onkol; 27(11):3-27 1981

Cancer morbidity indices in the Soviet Union are summarized. An overall intensive index for 1979 was 201.6 per 100,000. A total number of newly detected cancers exceeded 530,000. Cancer morbidity in urban population was by 21.8% greater than that in rural population. The increase of morbidity indices was recorded for rectal cancer, lung cancer in men, skin cancer, breast cancer, and lymphatic and hemato poietic neoplasms. The decrease of morbidity indices was recorded for lip cancer, stomach cancer, and cervical cancer. There were no changes in the morbidity indices for esophageal cancer and lung cancer in women. The growth of prevalence index was indicative of the efficacy of the system of of cancer detection and follow-up. The overall index of 1-yr mortality was 35.4%. Absolute number of patients who died of cancer reached 366,400. The decrease of mortality indices was recorded for stomach cancer and cervix cancer. The increase of mortality indices was recorded for cancers of the mouth, pharynx, esophagus, rectum, larynx, lungs, breast, and urinary organs. (12 Refs) (In RUS)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

5. ALCOHOL AND CANCER.

MacSween RN
Univ. Dept. Pathology, Western Infirmary, Glasgow, Scotland
Br Med Bull; 38(1):31-33 1982

Epidemiologic and experimental studies are reviewed. Heavy alcohol consumption is assessed as a prime carcinogen of the esophagus and the mouth, a contributor of some type to carcinogenesis of the pharynx and larynx, and a cause of primary hepatocellular carcinoma in conjunction with hepatic cirrhosis. Associations with cancer of other portions of the gastrointestinal tract, the breast, thyroid, kidney, and bladder are equivocal. The actual mode of action is not known; possibilities are discussed. (30 Refs)

6. SMOKING AS RISK FACTOR FOR DIFFERENT FORMS OF CANCER AMONG 26,000 MEN AND WOMEN IN NORWAY. MATCHING OF THE GROUP OF SMOKERS WITH THE CANCER REGISTRY OVER A 12-YEAR PERIOD.

Lund E, Zeiner-Henriksen T
Kreftregisteret, Montebello, Oslo 3, Norway
Tidsskr Nor Laegeforen; 101(34-36):1937-1940 1981

The cancer risk due to smoking was studied among 11,979 men and 13,998 women born between 1895 and 1929 on the basis of data in the Norwegian Cancer Registry for the period 1966-1977. A total of 1,815 cases of cancer were registered for this group during the studied period. Nonsmokers accounted for 22.4% among men and 76.5% among women, ex-smokers for 21.7% and 4.2%, current smokers for 55.4% and 19.1%, and the smoking habits of 0.5% of the men and of 0.2% of the women are unknown. The age-adjusted relative risk (relative

to nonsmokers) per 1,000 men was found to be 4.8 for lung cancer and 2.3 for cancer of the urinary bladder and urethra. For women, the relative risk was found to be 1.9 for lung cancer, 1.5 for cancer of the urinary bladder and urethra and 1.3% for cancer of the uterine cervix. The relative risk for all smokers was found to be 1.4 for lip cancer (men), 7.5 for stomach cancer (men), 4.4 for colon cancer (men), 0.9 for larynx cancer, 9.2 (men) and 1.7 (women) for lung cancer, 3.3 for cancer of the uterine cervix, 12.4 for prostate cancer, 3.7 (men) and 1.2 (women) for cancer of the urinary bladder and urethra, 4.8 (men) and 3.4 (women) for lymphoma and leukemia. Significant difference between smokers and nonsmokers was found with respect to laryngeal cancer (men), esophageal cancer (men), cancer of the liver and bile ducts (women) and carcinoma of the uterine cervix as well. The risk of cancer of the upper respiratory passages are higher for pipe smokers than for cigarette smokers, while cigarette smokers had higher risk of lung cancer than pipe smokers. The cancer risk was found to be lower among ex-smokers than current smokers, and it increased with cigarette consumption. (17 Refs) (In NOR)

7. CONCEPTS IN CAUSALITY: CHEMICALLY INDUCED HUMAN URINARY BLADDER CANCER.

Lower GM
Center Human Systems, Inst. Environmental Studies, Univ. Wisconsin, WARF Building, 610 Walnut St., Madison, WI, 53706
Cancer; 49(5):1056-1066 1982

A significant portion of the incidence of human urinary bladder cancer can be attributed to occupational and cultural (tobacco smoking) situations associated with exposures to various arylamines, many of which represent established human carcinogens. A brief historical overview of research in bladder cancer causality indicates that the identification of causal agents and causal mechanism has been approached and rests upon information gathered at the organismal (geographical/historical), cellular, and molecular levels of biologic organization. This viewpoint speaks of a natural evolution within the biomedical sciences; a natural evolution from descriptive approaches to mechanistic approaches; and a natural evolution from more or less independent discipline-oriented approaches to hierarchically organized multidisciplinary approaches. Available information relevant to bladder cancer causality can be readily integrated into general conceptual frameworks to yield a hierarchial view of the natural history of urinary bladder cancer, a view consistent with contemporary natural systems and information theory and perhaps relevant also to other chemically induced epithelial cancers. Such frameworks are useful in appreciating the spatial and temporal boundaries and interrelationships in causality and the conceptual interrelationships within the biomedical sciences. Recent approaches in molecular epidemiology and the assessment of relative individual susceptibility to bladder cancer indicate that such frameworks are useful in forming hypotheses. (Author abstract) (62 Refs)

8. OVERVIEW OF FINNISH EPIDEMIOLOGIC STUDIES ON OCCUPATIONAL CANCER.

Tola S
Dept. Epidemiology and Biometry, Inst. Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland
Scand J Work Environ Health; 7(Suppl4):133-139 1981

Finnish epidemiologic studies on occupational cancer are discussed with respect to asbestos, foundry work, rubber work, trichloroethylene, childhood cancer, bladder cancer, nasal cancer, and occupational mortality and cancer incidence statistics. Occupational mortality statistics for 1971-1975 revealed an excess cancer mortality among males for miners and quarry men and workers in industry. Among women excess cancer deaths were found for administrative, managerial, and clerical workers. Since smoking was relatively evenly distributed between different occupational groups, the differences in lung cancer incidence could not be explained only by smoking. Definite evidence of the association between cancer occurrence and asbestos and iron foundry work has been shown in Finland. Results in the rubber industry were similar to those obtained in other countries, but the material was small and had not reached statistical significance. The association between nasal carcinoma and the furniture industry is inconclusive because of the small number of cases. Large occupational cohorts may hide the increased risk of some special work groups. Some major impediments for the etiologic study of occupationally induced cancer in Finland include the small number of exposed workers, relatively short exposure periods, and the relatively recent establishment of many industries in the country. (33 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

9. STREPTOZOTOCIN INDUCED DIABETIC NEPHROPATHY AND RENAL TUMORS IN THE RAT.

Bleasel AF, Yong LC
Sch. Pathology, Univ. New South Wales, P.O. Box 1, Kensington, New South Wales, 2033, Australia
Experientia; 38(1):129-130 1982

Adult Wistar rats rendered diabetic by a single dose of streptozotocin develop renal morphological changes which show subtle differences compared to those seen in human diabetic renal disease. The early tubular degeneration is sited in the distal rather than the proximal convoluted tubule and subsequent glomerular lesion shows linear deposits of IgG and albumin in the basement membrane rather than in the mesangium. The carcinogenicity of streptozotocin in the rat is reconfirmed. (Author abstract) (17 Refs)

10. LIFETIME CARCINOGENICITY STUDY OF 1-AND 2-NAPHTHYLAMINE IN DOGS.

Purchase IF, Kalinowski AE, Ishmael J, Wilson J, Gore CW, Chart IS
Central Toxicology Lab., Imperial Chemical Industries Ltd., Alderly Park, Macclesfield, Cheshire, England
Br J Cancer; 44(6):892-901 1981

Groups of male and female beagle dogs were given daily doses of 400 mg of various mixtures of naphthylamines for up to 109 mo. Survivors were killed at 128 mo. A variety of pathologic conditions were diagnosed, but the only effect related to treatment was the induction of bladder neoplasms. All dogs which received pure 2-naphthylamine developed transitional-cell carcinomas of the bladder within 34 mo. Two of eight dogs receiving 6% 2-naphthylamine in 1-naphthylamine developed early carcinoma and two of eight dogs receiving 0.5% 2-naphthylamine in 1-naphthylamine developed hemangioma of the bladder. Some of the dogs receiving 1-naphthylamine (total dose 950 g) and the controls had focal cystitis or hyperplasia, but no neoplasia of the bladder. These results confirm the carcinogenicity of 2-naphthylamine to dogs. No carcinogenic effect of 1-naphthylamine was observed, indicating that it is at least 200x less potent as a carcinogen than 2-naphthylamine.

The incidence of bladder cancer in dogs fed mixtures of both naphthylamines explains why previous experimental and epidemiological studies of impure 1-naphthylamine have revealed carcinogenicity. (Author abstract) (22 Refs)

11. MORPHOLOGY OF NASAL CAVITY NEOPLASMS IN F-344 RATS AFTER CHRONIC FEEDING OF P-CRESIDINE, AN INTERMEDIATE OF DYES AND PIGMENTS.

Reznik G, Reznik-Schuller HM, Hayden DW, Russfield A, Murthy AS
Tumor Pathology Branch, NCI, NIH, Bethesda, MD, 20205
Anticancer Res; 1(5):279-286 1981

A chronic animal test of p-cresidine (CR: 2-methoxy-5-methylbenzenamine) was conducted to examine risk of cancer in the dye manufacturing industry. Fifty male and 50 female F-344 rats were used. CR was administered to the animals as a component of the diet (0.5 and 1.0%). Male and female rats weighed less than the respective controls. Significant positive association was observed between dosage and mortality. For male rats 62% of the high dose rats, 96% of the low dose rats, and 94% of the control rats survived at least 75 wk. For female rats, 76% of the high dose rats, 98% of the low dose rats, and 96% of the control rats survived at least 75 wk. Both male and female rats fed CR showed compound-related effects in the urinary bladder and in the epithelium of the nasal cavity. Dose-related carcinomas, adenomas, and papillomas were observed. Hyperplasia (HP) or squamous metaplasia (SMP) of the submucosal nasal glands or the epithelium was only dose related in female rats. In male rats the number with lesions was similar in both low and high doses. HP or SMP was multifocal in the nasal cavity. Adenomas were located in respiratory turbinals. Adenocarcinomas were poorly differentiated and consisted of masses of cells having scant cytoplasm and large, ovoid nuclei with prominent chromatin. In many tumors invading the brain, rosettes, pseudorosettes, or palisading of cells suggested neurogenic origin. The incidence of adenocarcinomas in females and males was higher in the high dose groups than in the controls; the tumors appeared as early as wk 48 in males and wk 62 in females. Results indicated that CR is carcinogenic, with administration resulting in increased incidence of adeno- and squamous cell carcinoma of the nasal cavity in rats. (19 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

12. AGE-RELATED CHANGES IN MUTAGEN ACTIVATION BY RAT TISSUES.

Robertson IG, Birnbaum LS
(c/o Birnbaum) Environmental Biology Branch, Natl. Inst. Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC, 27709
Chem Biol Interact; 38(2):243-252 1982

Age-related changes in drug metabolism of the liver, lung and kidney of adult female Long-Evans rats were determined by measuring changes in mutagen formation. Activation of aflatoxin B1 (AFB1), 2-aminofluorene (AF) and 2-acetylaminofluorene (AAF) to mutagenic derivatives was assayed using the Ames Salmonella test system. The promutagens were incubated with tissue fractions from rats ranging in age from 2.5 to 25 mo. With all three compounds, hepatic, renal and pulmonary activation was lower in the senescent than in the young adult animals. The largest decrease, however, occurred prior to middle-age, ie before 9-13 mo. In liver and kidney, little change was detectable between the middle-aged and the old (20-25 mo) animals. However, pulmonary metabolism in the oldest animals was slightly higher than in the extracts from the middle-aged rats. The observed decline in mutagen activation may thus be a function of maturation rather than senescence. (Author abstract) (30 Refs)

13. REACTIONS OF VINYL CHLORIDE WITH RNA AND DNA OF VARIOUS MOUSE TISSUES IN VIVO.

Bergman K
Toxicology Lab., Natl. Food Admin., Box 622, S-751 26 Uppsala, Sweden
Arch Toxicol; 49(2):117-129 1932

The irreversible binding of 14C-vinyl chloride metabolites to RNA and DNA of mouse brain, lung, liver, kidney, spleen, pancreas, and testes after a single ip injection has been studied. Hydrolysates of nucleic acids from selected organs were separated on Aminex A6 for quantitation of alkylation products. Radioactivity in nucleic acids was registered in all of the studied organs with the exception of brain. RNA from spleen, pancreas and liver, and DNA from spleen and liver contained the highest amounts of radioactivity. In nucleic acids from spleen and pancreas, both organs of high metabolic activity, the entire radioactivity was found metabolically incorporated as C1-fragments. In RNA of kidney and liver, a large part of the radioactivity was also present as incorporated C1-fragments, but 3,N4-ethenocytidine (in kidney) as well as 1,N6-ethenoadenosine and 1,N6-ethenoadenine (in kidney and liver) were identified as alkylation products. In liver DNA, incorporation of C1-fragments was insignificant, indicating different interactions of vinyl chloride metabolites (C1-fragments and alkylating products) with RNA and DNA. The elution profiles of radioactivity in hydrolysates of liver DNA were dominated by an alkylation product of unknown structure (probably a derivative of deoxyguanosine). Possibly, 1,N6-ethenodeoxyadenosine and 1,N6-ethenoadenine were also present in liver DNA. The results are consistent with the ability of vinyl chloride to act as a multipotent carcinogen by alkylation of DNA in several tissues. (Author abstract) (45 Refs)

14. CHEMICAL CARCINOGENS TRANSFORM BHK CELLS BY INDUCING A RECESSIVE MUTATION.

Bouck N, Di Mayorca G
Dept. Microbiology/Immunology, Northwestern Univ., Chicago, IL, 60611
Mol Cell Biol; 2(2):97-105 1982

Mechanisms of transformation (TF) by chemical carcinogens were studied in the baby hamster kidney cell line BHK-21 clone 13. Tumorigenic transformed cell lines were derived from BHK cells by exposure to papovavirus (PV), dimethylnitrosamine (DMN), nitrosomethylurea (NMU), or 4-nitroquinoline-N-oxide (4-NQO) or by spontaneous transformation. NMU or 4-NQO produced TF and mutations to 6-thioguanine-resistance (6-TGR) or ouabain-resistance (OR) in a dose-related fashion. Parallel dose-response curves for TF, 6-TGR, and OR suggested that TF and mutation occurred by similar mechanisms. Two frame-shift mutagens, ICR-170 and ICR-191, had dose-response curves for survival and TF that were identical. Both compounds produced temperature-restriction mutations in inverse proportion to frame-shift mutations. Fusion of transformed cells with isogeneic normal cells showed that TF in-

duced by PV behaved as a genetic dominant, but spontaneous or chemically induced TF behaved as a genetic recessive. These genetic patterns were exhibited soon after fusion and also after establishment of hybrid clones. All hybrids were nearly tetraploid. Hybrids showed segregation of TF; transformed phenotype was reexpressed in most cases in the form characteristic of the original transformed parent. Results indicate that chemical carcinogenesis in BHK cells involves induction of a recessive mutation as part of a multistage process. (58 Refs)

15. SERUM PROTEINS AND TUMOR MARKERS IN RENAL ARTERIAL AND VENOUS BLOOD IN PATIENTS WITH RENAL CANCER.

Hisazumi H, Nakajima K, Nishino A, Naito K, Kuroda K, Migita S, Konishi K
Dept. Urology, Sch. Medicine, Kanazawa Univ., Kanazawa, Japan
Hinyokika Kiyo; 27(10):1185-1193 1981

In vivo production of some serum proteins and tumor markers in renal cancer tissue, was investigated. Their concentrations in renal arterial and venous blood samples have been determined in 11 patients with renal cancer. In two other groups, one consisting of 13 renal cancer patients without metastasis and another 13 renal cancer patients with metastasis, pre- and post-operative changes of concentration of 36 serum proteins in peripheral blood have been studied as well. The 36 serum proteins were quantitatively determined by a micro-single radial immunodiffusion method described by Migita and five tumor markers, beta-human chorionic gonadotropin (beta-HCG), alpha-fetoprotein (AFP) ferritin, carcinoembryonic antigen (CEA) and beta-2 microglobulin (BMG), were determined using commercially available radioimmunoass ay kits. From the data obtained from the 11 patients, it was not possible to assure the production of any serum protein in renal cancerous tissue. A large variety of serum proteins showing a decrease of the concentration in renal venous blood had a relatively close relationship to patients with a large tumor lesion. A sporadic increase of several serum proteins in the venous blood was observed. Production of beta-HCG, BMG and ferritin in renal cancerous tissue was strongly suggested in one, one and five patients, respectively. In the group of 13 patients without metastasis, abnormal levels of Alb, alpha1AT, alpha1AG, Hp, C9 and Hx returned to a normal range after nephrectomy, and these post-operative alpha1AT, alpha1AG, Hp and Hx levels showed a significant difference as compared with post-operative levels of those proteins in the 13 patients with metastasis. These results suggested that post-operative changes of the four serum proteins would be a useful parameter for the occurrence of a deteriorating event in the subsequent course, eg, tumor recurrence or metastasis development. (25 Refs) (In JPN)

16. A VARIANT ALKALINE PHOSPHATASE IN RENAL CELL CARCINOMA.

Whitaker KB, Eckland D, Hodgson HJ, Saverymuttu S, Williams G, Moss DW
(c/o Moss) Dept. Chemical Pathology, Royal Postgraduate Medical Sch., Hammersmith Hosp., London W12 OHS, England
Clin Chem; 28(2):374-377 1982

We report a case of renal cell carcinoma in which up to 32% of the abnormally increased alkaline phosphatase activity in serum was contributed by a variant alkaline phosphatase originating in the primary tumor and its secondary deposits. The variant enzyme was probably an altered form of normal renal alkaline phosphatase. The rest of the alkaline phosphatase activity in the serum was of hepatic origin, but no abnormality of the liver was discovered at autopsy. (Author abstract) (15 Refs)

17. SERUM PROTEIN PROFILES IN CARCINOMA OF THE KIDNEY.

Richards B, Robinson MR, Pidcock NB, Cooper EH
York District Hosp., York, England
Eur Urol; 8(1):32-36 1982

The levels of serum acute phase reactant proteins (APRPs) have been examined in untreated kidney carcinoma and during the evolution of metastases. These proteins can provide a warning of the likelihood of extensive local or metastatic spread at first presentation. The levels of APRPs rise with increasing tumor burden but the system is insensitive to small tumor burdens. Beta2-Microglobulin levels do not contribute additional information. Serum phosphohexose isomerase tends to be elevated when there is a large tumor burden but its change does not accurately mirror the rate of expansion of the tumor. The APRPs and phosphohexose isomerase are useful in alerting the clinician to the probability of metastases or large local masses in kidney cancer, but have a limited use in monitoring. (Author abstract) (17 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

18. TISSUE-SPECIFICITY OF N-NITROSODIBUTYLAMINE METABOLISM IN SPRAGUE-DAWLEY RATS.

Brittebo EB, Tjalve H
Dept. Toxicology, Univ. Uppsala, Box 573, S-751 23 Uppsala, Sweden
Chem Biol Interact; 38(2):231-242 1982

The distribution and metabolism of N-[14C]nitrosodibutylamine were studied in Sprague-Dawley rats. The results indicated that in addition to the liver, metabolism of the substance occurred in the nasal mucosa, the lung and the esophagus. Metyrapone and diethyldithiocarbamate reduced the production of 14CO2 from N-[14C]nitrosodibutylamine by all these tissues. There was no indication of metabolic capacity in the urinary bladder or the kidney. The results fit with the assumption that tumors of the urinary tract are induced by metabolites reaching these tissues via the urine. Besides the liver, the esophagus and the lung are target tissues for the carcinogenicity of N-nitrosodibutylamine in Sprague-Dawley rats and in these tissues the local formation of reactive metabolites may play a role in the pathogenesis of N-nitrosodibutylamine-induced lesions. (Author abstract) (21 Refs)

19. ULTRASTRUCTURAL CHANGES IN SURFACE TOPOGRAPHY, GLYCOCALYX AND PLASMA MEMBRANE INTERIOR OF TUMOR CELLS DURING EXOCYTOSIS OF MUCUS.

Alroy J, Ucci AA, Roganovic D, Jacobs JB, Merk FB
Dept. Pathology, Tufts Univ. Sch. Medicine and Veterinary Medicine, Boston, MA, 02111
J Submicrosc Cytol; 14(1):171-177 1982

Plasma membrane changes, which occur during exocytosis, were studied by electron microscopy in six specimens of pri-

mary mucous-producing adenocarcinoma of human urinary bladder. The luminal surfaces of non-secretory neoplastic cells display numerous microvilli, which have a thick ruthenium red-positive glycocalyx. Neoplastic secretory cells have a smooth luminal surface with relatively few microvilli. The glycocalyces of these cells are thin, especially at locations where the plasmalemma and underlying mucous granule membrane are in close opposition. The fused membranes often bulge into the lumen forming distinct protuberances. In freeze-fracture replicas the protuberances appear devoid of 7-8 mm intramembrane particles. Our results suggest that there are differences between non-secretory and secretory neoplastic cells that are expressed in surface topography, glycocalyx and internal membrane structure. Secretion-induced changes observed in plasma membranes of the neoplastic cells closely resemble changes that are known to occur in the plasmalemma of normal secretory cells. (Author abstract) (18 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

20. STUDIES OF CAUSAL CORRELATIONS AND PATHOGENESIS OF LEUKOSIS, NEPHROBLASTOMAS, OVARIAN TUMORS, AND OSTEOPETROSIS AFTER INFECTION WITH AVIAN LEUKOSIS VIRUSES.

Loliger HC, Von dem Hagen D, Hartmann W
Institut fur Kleintierzucht, D-3100 Celle, W. Germany
DTW; 89(1):22-28 1982

Correlations between infection with avian leukosis viruses and appearance of leukosis (LK), nephroblastomas (NB), ovarian tumors (OT), and osteopetrosis were studied. Several lines of chickens with varying viral sensitivities were infected with avian myeloblastosis virus (AMV), avian erythroblastosis virus (AEV), or Marek herpes virus (MHV). Pathological conditions developed in chickens susceptible to A- or B-group avian leukosis viruses (ALV) but not in resistant chickens. Pleiomorphic diseases developed in chickens infected with AMV but not in chickens infected with MHV or AEV. MHV induced only monomorphic lymphoreticular neoplasias; induction was independent of the stage of genetic susceptibility. The incidence of pathological conditions decreased as the age of chickens at the time of infection increased. In older chickens leukemia appeared only as acute, early stages of disease. Occurrence of leukemia was related to the concentration of virus introduced. Nephroblastomas and cystadenomas appeared as late effects of viral infection and increased in frequency as the frequency of acute leukemia decreased. Osteopetrosis developed in all lines susceptible to AMV, particularly in dysgammaglobulinemic lines. No association of nephrogenic or osteogenic tumor factor with viruses of subgroup A or B was demonstrated. Results indicate that the targets of AMV are pluripotential embryo-reticular cells and undifferentiated hemoblast present only in newly hatched chicks, and that the viruses act by blocking cellular differentiation. (25 Refs) (In GER)

21. INTEGRATION AND EXPRESSION OF VIRAL DNA IN CELLS TRANSFORMED BY HOST RANGE MUTANTS OF ADENOVIRUS TYPE 5.

Ruben M, Bacchetti S, Graham FL
(c/o Graham) Dept. Pathology and Biology, McMaster Univ., Hamilton, Ontario L8N 3Z5, Canada
J Virol; 41(2):674-585 1982

Group I host range (hr) mutants of adenovirus Type 5 are unable to transform rat embryo or rat embryo brain cells but induce an abnormal transformation of baby rat kidney cells. We established several transformed rat kidney cell lines and characterized them with respect to the transformed phenotype and the structure of the integrated viral DNA. The hr mutant-transformed cells, unlike wild-type virus transformants, were fibroblastic rather than epithelial, failed to grow in soft agar, and were also less tumorigenic in nude mice. Studies on the structure of the integrated viral DNA sequences showed that hr-transformed cells always contained the left end of the adenovirus DNA, but the size of the integrated DNA fragment varied among different lines, and a high percentage of the lines contained the entire viral genome colinearly integrated. The patterns of integration were maintained after prolonged growth in culture an d after subcloning. Attempts to rescue infectious virus from lines which contained the entire genome were unsuccessful. Using immunoprecipitation and sodium dodecyl sulfate-polyacrylamide gel electrophoresis, we analyzed the viral proteins expressed in hr-transformed cells. Results of these studies indicated that, like wild type-transformed cells, hr transformants expressed E1B proteins of mol wt 58,000 and 19,000. (Author abstract) (48 Refs)

22. MONOCLONAL ANTIBODIES TO TWO MOUSE BLADDER CARCINOMA ANTIGENS.

Hellstrom I, Rollins N, Settle S, Chapman P, Chapman WH, Hellstrom KE
Program Tumor Immunology, Fred Hutchinson Cancer Res. Center, Seattle, WA, 98104
Int J Cancer; 29(2):175-180 1982

Carcinomas of the urinary bladder of mice were induced by 3-methyl-cholanthrene or FANFT [(4-5-nitro-2-furyl)-2-thioazolyl formamide]. On transplantation in vivo, tumor lines consisting of well-differentiated transitional-cell carcinomas were established. Some tumors were also explanted in vitro. A rat was immunized with a pool of carcinomas and normal bladder tissue and its spleen cells were hybridized with NS-1 mouse myeloma cells. Supernatants of hybrid cells ('hybridomas') were screened for antibody binding to antigens present in bladder carcinomas but not in normal syngeneic urinary bladder, with cell extracts as targets. Hybridomas that appeared to have the required specificity were cloned, tested further against transitional-cell bladder carcinomas, an anaplastic bladder tumor, rhabdomyosarcomas, a mammary carcinoma, myelomas and lymphomas, and normal adult urinary bladder, kidney, lung, spleen, heart, brain, thymus, and whole embryo. Antibody formed by one hybridoma, 2H5, gave significant binding to membranes from five of seven transitional-cell carcinomas but not to membranes from any other tissues. A second hybridoma, IE6, formed antibody to an antigen present in bladder carcinomas and normal liver and, in smaller amounts, in several other normal and neoplastic tissues. Fluorescence microscopy established that both antigens were present at the cell surface of transitional-cell bladder carcinomas. Immunoprecipitation and SDS-polyacrylamide gel electrophoresis were used to identify the target antigens from 125I-labeled cell membrane proteins. The antibody formed by 2H5 was

found to identify a protein with a mol wt in the range of 140 kilodaltons, which was detected in transitional-cell bladder carcinoma and, in small amounts, in normal bladder. The molecular nature of the antigen defined by hybridoma IE6 is not known. (Author abstract) (25 Refs)

23. CELL SURFACE ANTIGEN - A STUDY IN BLADDER TUMOURS.

Kulkarni JN, Kamat MR, Gangal SG, Talwalkar GV
G.U. Service, Tata Memorial Hosp., Bombay, India
J Surg Oncol; 19(1):14-17 1982

Thirty bladder tumors of various stages and grades were examined for the presenc e of ABO (H) cell surface antigen using specific red cell adherence (SCRA) technique. Ten patients with Stage A disease and low grade tumor (Grade I) retained the antigens, whereas all patients with high stage disease (B,C,D) and high grade tumors showed absence of antigen. When these data were correlated with recurrence pattern and metastasis or invasion rate, patients who did not show the antigen at the initial visit developed metastases and had poor prognoses. The patient who had expressed the antigen by positive SCRA had fewer recurrences and a longer tumor-free interval. Hence if SCRA is done in all bladder tumors at the initial visit and at subsequent follow-up, it can be used as a biological marker. (Author abstract) (7 Refs)

24. BLOOD GROUP ABO (H) CELL SURFACE ANTIGENS IN BLADDER TUMORS INVADING THE CHORION. THE PROGNOSTIC VALUE OF THEIR DETERMINATION BY IMMUNOFLUORESCENCE. A RETROSPECTIVE STUDY OF 125 CASES.

Vacant J, Le Portz B, Augustin I, Hammou JC, Fella C, Delignieres S, Maiolini R, Masseyeff R, Abelanet R, Steg A
GRET, G.I.E. FAX, 5, rue Eugene Emmanuel, 06000 Nice, France
Ann Urol (Paris); 16(1):24-29 1982

In a group of 125 patients with Stage A bladder tumors, antigens of the AB and H blood group were collected and studied. All patients were studied after a follow-up of at least 5 yr. In 18 patients there was no recurrence. In 20 patients, there was Stage A recurrence, and in 76 patients there was at least Stage B recurrence. In 11 cases, the condition was uncertain. In the group of 11 patients whose tumor cells were immunofluorescent positive, all were alive at 5 yr follow up and all except one were free of all tumors. In the group of 37 patients who had a positive but heterogeneous immunofluorescence, 14 patients (37.8%) were alive at 5 yr follow up and 23 had died. Of 77 patients whose cells all tested negative, 20 patients (27%) were alive at 5 yr and 8 of these had no recurrence. It is suggested that homogeneous retention of the surface antigens is a favorable prognostic indicator even if the tumor has already infiltrated the chorion. Although the disappearance of surface antigens had been proven to be adverse, the significance has not yet been established. (27 Refs) (In FRE)

25. A STUDY OF THE DISTRIBUTION OF ABH CELL SURFACE ANTIGENS IN BLADDER TUMORS BY INDIRECT IMMUNOFLUORESCENCE.

Vallancien G, Rouger P, Leclerc JP, Kuss R
Clinique Urologique, Hopital de La Pitie, 83, boulevard de l'Hopital, 75634 Paris, France
Ann Urol (Paris); 16(1):30-33 1982

In a study of 30 patients with bladder tumors (transitional cell epitheliomas), only three cases (10%) retained A, B, or H antigens on the urothelium. In a control group of 30 patients with healthy bladders, antigens were present in all cases. Four types of distribution of A, B, and H an tigens were found. There was no correlation between tumor stage or grade and the type of immunofluorescent distribution. Absence of fluorescence of the tumor epithelium was found in 10/17 of the Grade I tumors. None of these tumors enolved toward muscle infiltration. In 4/5 cases of Grade II or III tumors, there was absence of fluorescence, and invasion or infiltration of the muscle occurred. Of 18 histologically, superficial tumors which invaded only the mucous membrane, four lost antigens and evolved toward muscle infiltration. Two tumors which were positive recurred in the same superficial stage. In the other cases, the tumor lost all or part of its antigenicity and evolved toward the infiltration of muscle. Infiltration of the muscle occurred in 3/8 Stage I tumors which were completely negative. The other five lost part of their antigens, but none evolved to muscle infiltration. Although the loss of ABH antigens did not seem to be associated with tumor grade or stage, the persistence of the ABH antigens was considered a favorable prognostic factor. (17 Refs) (In FRE)

26. THE USE OF IMMUNOFLUORESCENCE FOR IDENTIFYING ABH CELL SURFACE ANTIGENS IN FROZEN BLADDER SECTIONS.

Devonec M, Blanc-Brunat N, Bouvier R, Muchada E, Dubernard JM
Service d'Urologie, Pavillon v, hopital Edouard Herriot, place d'Arsonval, Lyons, France
Ann Urol (Paris); 16(1):34-39 1982

The results of an immunofluorescent study of 24 patients with initial or recurrent bladder tumors were compared with six controls having normal mucous membranes. All of the controls presented the same characteristics with homogeneous fluorescence limited by the basal membrane. The fluorescence was limited to membranes and did not include the cytoplasm. Antigenic expression was always completely loss in carcinoma in situ. Papillary lesions also lost antigenic expression. In certain hyperplastic states, fluorescence disappears from the basal to the more superficial layers. In carcinoma in situ and papillary lesions the fluorescence was limited to the basal membrane. When histological examinations were correlated with fluorescent results, the transition between healthy epithelium and the mucosa of carcinoma in situ or papillary lesions could be determined by a loss of normal antigenic expression as fluorescence diminished in the areas of the tumors. Since microscopic interpretation was considered too subjective a method of interpretation, flow cytometry is recommended as the most appropriate tool for fluorescent study. (14 Refs) (In FRE)

27. IMMUNOFLUORESCENCE AS A MEANS OF IDENTIFYING ABH CELL SURFACE ANTIGENS IN UROTHELIAL CELLS FROM BLADDER IRRIGATION FLUID.

Devonec M, Fontaniere B, Blanc-Brunat N, Muchada E, Sarkissian J, Dubernard JM
Service d'Urologie, Pavillon V, Hopital Edouard Herriot, place d'Arsonval, 69374 Lyon, France
Ann Urol (Paris); 16(1):40-43 1982

The results of an immunofluorescent study of 24 patients with initial or recurrent bladder tumors were compared with six controls having normal mucous membranes. In the control group basal cells and intermediary cells from bladder irrigations displayed intense fluorescence. The superficial cells in the washings displayed either little or no fluorescence. In washings from cancer patients, leukocytes and evidence of bleeding in

numerous urothelial cells revealed associated hemorrhagic conditions or infections. The loss of antigenic expression (AE) appeared directly related to the neoplastic character of certain cells. The normal cells from the washings were used as reference cells and defined the degree of normal AE. Surrounding neoplastic cells lost all AE in their membranes. The fluorescence which they presented was a nonspecific, autofluorescence of the cytoplasm. Since the loss of AE occurs in aging cells, the interpretation AE for diagnostic purposes in bladder cancer is recommended only insofar as certain conditions are met. These conditions include an estimate of cell viability and a precise measurement of the normal membrane fluorescence. (7 Refs) (In FRE)

28. EVALUATION OF ANTIBODY-DEPENDENT CELL CYTOTOXICITY (ADCC) AND SPONTANEOUS LYMPHOCYTE-MEDIATED CYTOTOXICITY (SLMC) IN PATIENTS SUFFERING FROM MALIGNANT DISEASE.

Degliantoni G, Mangoni L, Manna A, Funcini M
Cattedra di Ematologia - Clinica Medica Generale e Terapia Medica, Universita degli Studi di Parma, Parma, Italy
G Clin Med; 62(9):609-623 1981

The immune system and the evolution of malignant neoplasia were studied in 36 patients with cancer. Lymphocytes B, T, and EA rosette formation were determined in normal controls (NC: 20-70 yr old patients) with different diseases (DD), with localized cancer (LC: pulmonary, mammary, digestive tract, melanomas etc), with metastasizing cancer (MC: mammary cancer with bone and brain metastases, colon cancer with hepatic metastases and bladder cancer with bone and lymph node metastases), patients receiving polychemotherapy (PCT) with 5-fluorouracil and dacarbazine, patients receiving cyclophosphamide (CYP), and patients receiving radiotherapy (RT). Antibody-dependent cell cytotoxicity (ADCC) and spontaneous lymphocyte-mediated cytotoxicity (SLMC) were present in all NC with values slightly lower in older persons and women. The values for lymphocytes B, T, and EA rosette for NC were on the av 10%, 55%, and 8%, respectively, for DD the values were 8%, 53%, and 7% respectively, for not treated LC the values were 7%, 47%, and 7%, respectively, for not treated MC were 8%, 41%, and 6% respectively, for PCT were 7%, 38%, and 6%, respectively, for treated with CYP the values were 4%, 22%, and 3%,respectively, and for treated with RT the va lues 2%, 7%, and 2%, respectively. Natural Killer cell activity was significantly decreased in MC patients. Differences of lytic response in vitro were not related to T/B lymphocyte ratio in 90% of the cases. (5 Refs) (In ITA)

REVIEWS AND OTHER RELATED STUDIES

29. BLADDER CANCER.

Skrabanek P, Walsh A
Endocrine Oncology Unit, Mater Misericordiae Hosp., Dublin, Ireland
UICC Tech Rep Ser 60: 192 pp., 1981.

Data on the etiological factors, pathology, and biology of bladder cancer are summarized. Influence of the data on treatment is indicated and ideas for further research are collated. Topics discussed include pathology (classification, metastatic spread in fatal cases, pathogenesis and histogenesis, ultrastructural studies, cytology), carcinoma in situ (definition, description, cystoscopic appearances, natural history, clinical presentation, therapy, other problems), endocrinology (diffuse endocrine system, peptidergic nervous system, paraneoplastic endocrinopathies), experimental models (animal models, bladder cells in culture), clinical and experimental aspects of therapy (superficial and invasive bladder cancer), clinical biochemistry and monitoring (biochemical tests, humoral and cellular immunity), etiology of bilharzial bladder cancer in Egypt, etiology (occupational carcinogens, tobacco and smoking, dietary factors, drugs, endogenous factors). (682 Refs)

30. RECENT ADVANCES IN CANCER CYTOGENETICS.

Pogosiants EE
All-Union Cancer Res. Center, Moscow, USSR
Genetika; 17(12):2087-2099 1981

Recent studies in the field of cancer cytogenetics are reviewed with special emphasis on karyotypic changes in leukemia and carcinoma cells, prezygotic chromosome mutations specific for certain human tumors, and phenomena of gene amplification characteristic for a number of tumors and for cells resistant to antineoplastic agents. Specific karyotypic changes were observed in human and murine leukemias, as well as in a number of experimental sarcomas and carcinomas. Specific involvement of chromosome 15 was recorded in murine radiation-induced and carcinogen-induced T-cell leukemias; also, trisomy for chromosome 15 or translocation involving chromosome 15 were detected in B-cell leukemias and lymphomas. Specific involvement of the distal third of chromosome 15 indicated that this region contains the cluster of genes responsible for normal differentiation and malignant transformation of lymphoreticular cells. Specific prezygotic chromosome aberrations were observed in retinoblastoma (deletion in the long arm of chromosome 13), nephroblastoma (deletion in the short arm of chromosome 11), and in familial kidney carcinoma (translocation between chromosomes 3 and 8). Specific resistance of eukaryotic cells to methotrexate was shown to be associated with the presence of homogenously stained regions and the number of double microchrom osomes. (73 Refs) (In RUS)

31. THE SMOKING-INDUCED EPIDEMIC.

Doll R
Green Coll. Oxford, Oxford, England
Can J Public Health; 72(6):372-381 1981

Review of smoking-induced diseases and influence of smoking on cancer is presented. Harmful effects of smoking are demonstrated by the results of the large follow-up studies of men with defined smoking habits that have been carried out in many countries. Results of the studies are presented showing the mortality in regular cigarette smokers, standardized for age relative to that in life-long non-smokers. Causes of death for which smoking is responsible include cancers of the mouth, tongue, oropharynx, esophagus, larynx, lung, bladder, possibly the kidney, and probably the pancreas, chronic bronchitis and emphysema, pulmonary heart disease, myocardial infarction, aortic aneurysm, and a wide variety of other vascular diseases. Data on mortality from lung cancer by sex, mortality of regular cigarette smokers relative to non-smokers for women, characteristics of smokers by age, sex ratio of mortality rates in British doctors, relative risk of death by cause in non-smoking women by smoking habit of husband, incidence of lung cancer and vitamin A consumption, relative risks of developing various cancers in relation to serum retinol levels, and mortality of cigarette smoking by type smoked are presented. Mortality from lung cancer in women who are non-smokers is increased if they are married to men who smoke suggesting that the health of non-smokers is liable to be damaged by other people's

smoke in public places. After confirmation of the new evidence smoking will then cease to be matter of concern only to the individual and his own family and will have to be classed together with other atmospheric pollution. (42 Refs)

32. CHEMICAL CARCINOGENESIS AND SMOKING.

Farber E
Dept. Pathology, Univ. Toronto, Banting Inst., 100 College St., Toronto, Ontario M5G 1L5, Canada
Can J Public Health; 72(6):381-385 1981

Development of cancer in the respiratory tract in relation to some of the steps for carcinogenesis is reviewed. Metabolic activation of the majority of the known carcinogens is a prerequisite for interactions with DNA and other cellular components. Genetic defects in repair processes in cells may lead to increase in sensitivity to some carcinogenic influences, and the role of cell proliferation is important. The next step in carcinogenesis is promotion, the selective stimulation of initiated cells to grow. Suggested mechanisms of promotion are differential inhibition, stimulation, necrosis with regeneration, and recovery. Regression or maturation to normal-appearing tissue appears to be entirely dependent on the environment. Persistence of focal proliferations with a greatly increased risk for development of a second f ocal change is considered to be the first neoplastic step. Important component of cancer development with smoking is the promoting effect of components in the smoke. Later precancerous changes characterized by cytologic and histologic alterations show biological reversibility. Studies indicated a presence of a distinctive enzyme and other markers very early in carcinogenesis and long before any cytologic evidence of alteration appears. In the bladder, the early cells in man and in animals show changes in staining for alkaline phosphatase. The observations point to the possibility of developing characteristic staining procedures that should enable the identification of early preneoplastic or premalignant changes in bronchial epithelial cells. (30 Refs)

* U. S. GOVERNMENT PRINTING OFFICE: 1982—361-842/121

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. AN EVALUATION OF THE GENETIC TOXICITY OF EPICHLORHYDRIN. A REPORT OF AN EXPERT GROUP OF THE INTERNATIONAL COMMISSION FOR PROTECTION AGAINST ENVIRONMENTAL MUTAGENS AND CARCINOGENS.
Sram RJ, Tomatis L, Bridges BA, Clemmesen J
(c/o Lohman), Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 87(3):299-319 1981

2. ETHYLENE DIBROMIDE (EDB). (REVISED).
NIOSH Document Development Branch
Robert A. Taft Lab., National Inst. Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, OH, 45226
Curr Intell Bull NIOSH (37): 13 pp., 1981.

3. CHEMICAL CARCINOGENESIS AND SMOKING.
Farber E
Dept. Pathology, Univ. Toronto, Banting Inst., 100 College St., Toronto, Ontario M5G 1L5, Canada
Can J Public Health; 72(6):381-385 1981

RADIATION CARCINOGENESIS

4. CELLULAR TRANSFORMATION BY RADIATION: INDUCTION, PROMOTION, AND INHIBITION.
Borek C
Radiological Res. Lab., Cancer Center/Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Supramol Struct Cell Biochem; 16(4):311-336 1981

5. EFFECTS OF IONIZING RADIATION ON THE DEVELOPING EMBRYO AND FETUS: A REVIEW.
Hoffman DA, Felten RP, Cyr WH
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Effects of Ionizing Radiation on the Developing Embryo and Fetus: A Review. Available from National Technical Information Service, Springfield, VA, as PB82-115379:, 160 pp., 1981.

DIETARY FACTORS IN CARCINOGENESIS

6. BETA-CARBOLINES, PSYCHOACTIVE COMPOUNDS IN THE MAMMALIAN BODY.
Airaksinen MM, Kari I
Dept. Pharmacology, Univ. Kuopio, P.O. Box 138, SF-70101 Kuopio 10, Finland
Med Biol; 59(4):190-211 1981

7. DIET AND CANCER OF THE LARGE BOWEL.
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Nutr Cancer; 2(4):241-249 1981

8. INFLUENCE OF DIET ON MAMMARY CANCER.
Carroll KK
Dept. Biochemistry, Univ. Western Ontario, London, Ontario, N6A 5C1, Canada
Nutr Cancer; 2(4):232-236 1981

9. ARTIFICIAL SWEETENERS IN RELATION TO THE EPIDEMIOLOGY OF BLADDER CANCER.
Howe GR, Burch JD
NCI Canada Epidemiology Unit, Univ. Toronto, Ontario, Canada
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EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

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Dept. Carcinostasis Res., Tokyo Univ. Medical Res. Inst., 4-6-1 Kindai, Minato-ku, Tokyo 108, Japan
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James WP, Bingham SA, Cole TJ
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Nutr Cancer; 2(4):203-212 1981

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Takemura N
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In JPN

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Dept. Biochemistry, Brandeis Univ., Waltham, MA, 02254
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Inst. General Pathology, Univ. Milan, 20133 Milan, Italy
Adv Cancer Res; 35:151-268 1981

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. EPIDEMIOLOGY OF UROLOGICAL TUMORS.

Winz R
Urologische Abteilung, Krankenhaus der Missionsschwestern, Burgwall 64, 4400 Munster-Hiltrup, W. Germany
Therapiewoche; 32(5):439-440,443 1982

Statistical analysis of mortality resulting from urological tumors in West Germany for a 10-yr period indicates that rates are increasing for all tumor types. Among tumors affecting both sexes bladder tumors were the most common (41,826 deaths), followed by renal tumors (29,836 deaths). An increase in testicular tumors was interrupted by a 2-yr decline; the peak mortality has shifted from the 25-30-yr to the 35-40-yr age group. Carcinoma of the prostate was the most frequent urological tumor (67,049 deaths). (no Refs) (In GER)

2. NEONATAL EMBRYONAL RHABDOMYOSARCOMA OF THE BLADDER. A CLINICO-PATHOLOGICAL CASE REPORT AND EPIDEMIOLOGICAL STUDY.

Harvey JM, Scott JM
Dept. Genito-Urinary Medicine, Glasgow Royal Maternity Hosp., 67 Black St., Glasgow, Scotland
Scott Med J; 27(1):52-57 1982

A case report of neonatal rhabdomyosarcoma of the bladder is described. The literature reveals only one other report nearly 40 yr previously. The epidemiological study of childhood rhabdomyosarcoma of the bladder shows a greater incidence in Scotland compared to the United Kingdom as a whole. (Author abstract) (14 Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

3. NEPHROBLASTOMA ASSOCIATED WITH MESANGIOPROLIFERATIVE GLOMERULONEPHRITIS.

Ringert RH, Pistor K
Oberarzt der Urologischen Universitatsklinik der GHS Essen, Hufelandstrasse 55, D-4300 Essen 1, W. Germany
Eur Urol; 8(2):125-126 1982

The case of a girl showing left-sided Wilms tumor together with a nephrotic syndrome is presented. Recovery after tumor nephrectomy was uneventful. After cessation of cytostatic chemotherapy chronic renal failure developed. Open wedge biopsy of the right kidney revealed endstage glomerular disease. Renal histology in patients with this rare combination and in those presenting with male pseudohermaphroditism and nephron disorders shows a specific pattern. It is suggested that there is a genuine type of nephropathy linked either to Wilms' tumor and/or to male pseudohermaphroditism. (Author abstract) (10 Refs)

4. EPIDEMIOLOGIC STUDY OF REFINERY AND CHEMICAL PLANT WORKERS.

Hanis NM, Holmes TM, Shallenberger LG, Jones KE
Exxon Corporation, P.O. Box 235, E. Millstone, NJ, 08873
JOM; 24(3):203-212 1982

A dynamic retrospective cohort study was performed to examine the mortality experience of workers at Exxon's Baton Rouge, La, refinery and chemical plant. Included were 8,666 regular employees who worked at least 1 mo during the period January 1, 1970 through Dec 31, 1977, and retirees who were alive as of Jan 1, 1970. Mortality from all causes of death was lower than expected when compared with that of the U S population of similar age, sex, and race. Analyses of mortality by specific site of cancer revealed elevated standardized mortality ratios (SMRs) for cancer of the kidney, testis, brain/central nervous system, pancreas, and lymphopoietic sites; none of these elevations was statistically significant. Because of the higher than av mortality from cancer of the pancreas in some Louisiana parishes and the observation that one additional death from cancer of the pancreas in this study would have resulted in a statistically significant SMR at the 95% confidence level, some emphasis was placed on this finding. No evidence was found to link cancer of the pancreas to a specific occupational group. An examination of mortality by occupational class revealed some elevated SMRs for further study. (Author abstract) (24 Refs)

5. A CASE OF BLADDER TUMOR SEEMED TO BE ASSOCIATED WITH CYCLOPHOSPHAMIDE.

Kato Y, Tsujihashi H, Matsuura T, Kaneko S, Iguchi M, Akiyama T
Dept. Urology, Kinki Univ. Sch. Medicine, Japan
Hinyokika Kiyo; 27(11):1383-1387 1981

A 54-year-old woman was diagnosed as Hodgkin's disease in 1979, and treated with cyclophosphamide, vincristine, vinblastine and prednisolone for a year. She was given a total dose 18g cyclophosphamide 50 mg daily. Hemorrhagic cystitis appeared 10 months after the beginning of the therapy and recurrent hematuria persisted for 3 months. Therefore cyclophosphamide was discontinued. One month after the cessation, necrotic tissues which contained many cells seemed to be malignant were discharged in the urine. Since cystoscopy revealed a broad based bladder tumor on the posterior wall, the tumor was resected transurethrally. Histological examination of the specimens did not ascertain the diagnosis of bladder carcinoma. Three months after the operation bladder tumor appeared again, and had no malignancy in histopathologic examination. However we think this case may have a malignant feature in future because of its recurrent character, and should be followed up very carefully. (Author abstract) (16 Refs) (In JPN)

6. MORTALITY AMONG PVC-FABRICATING EMPLOYEES.

Chiazze L, Ference LD
Div. Biostatistics and Epidemiology, Georgetown Univ. Sch. Medicine, 3750 Reservoir Road, N. W., Washington, DC, 20007
Environ Health Perspect; 41:137-143 1981

Causes of deaths among 3,847 white active and retired workers in 17 plants producing polyvinyl chloride (PVC) which occurred during the period 1964-1973 were studied. Proportionate mortality ratios (PMR) were calculated for various causes and compared with two standards: (1) the age-, sex-, and cause-specific mortality ratio for whites in 1968 and (2) mortality rates for the individual years 1964-1973. When compared with the 1968 standard, PMR for white males were significantly increased for the categories 'all cancers,' 'digestive cancers,' 'respiratory cancers,' and 'other and unspecified cancers.' PMR for white females were significantly increased for the categories 'all cancers,' 'digestive cancers,' 'breast cancer,' 'urinary cancer,' and 'other and unspecified cancers.' When compared with standards for individual years, results were consistent with those for the 1968 standard but PMR were generally

lower. Case-control analysis of 44 deaths due to breast cancer suggested an increased risk among PVC workers; the actual increase was not significant, possibly due to sample size. Analysis of sampling methods indicated that the study was capable of detecting only large increases in risk. (14 Refs)

7. AN INDEPENDENT ANALYSIS OF THE NATIONAL CANCER INSTITUTE STUDY ON NON-NUTRITIVE SWEETENERS AND BLADDER CANCER.

Walker AM, Dreyer NA, Friedlander E, Loughlin J, Rothman KJ, Kohn HI
(c/o Dreyer), Epidemiology Resources, Inc., P. O. Box 57, Chestnut Hill, MA, 02167
Am J Public Health; 72(4):376-381 1982

We evaluated the possible relation between use of non-nutritive sweeteners and bladder cancer using data obtained from the National Cancer Institute Bladder Cancer Study under the Freedom of Information Act. In the general study group, there was no evidence for an association between non-nutritive sweeteners and bladder cancer. Control for a variety of factors through multivariate techniques diminished the plausibility of earlier interpretations of these data, which had raised the possibility that certain subgroups of users of non-nutritive sweeteners might be at an increased risk for bladder cancer. We found that the putative effects of non-nutritive sweeteners were not consistent among subgroups with similar baseline risk, did not display consistent dose-response trends, and were subject to considerable sampling error. We concluded that the data provided little evidence that non-nutritive sweeteners increase risk for bladder cancer among subgroups of users, and that definitive evidence on this question is beyond the reach of conventional research. (Author abstract) (2 Refs)

8. NON-NUTRITIVE SWEETENERS AND BLADDER CANCER.

Hoover R, Hartge P
Environmental Epidemiology Branch, NCI, NIH, Landow Building 3C07, Bethesda, MD, 20205
Am J Public Health; 72(4):382-383 1982

A recent report by Walker et al re-evaluating an NCI study revealed no association between bladder cancer risk and past consumption of artificial sweeteners in the total study population. Certain procedures of this study were criticized, including omission of design variables (sex and age) from generation of risk scores and statements concerning the role of epidemiology in assessing low-level risks. (5 Refs)

9. A STUDY ON THE ETIOLOGICAL FACTORS OF BILHARZIAL BLADDER CANCER IN EGYPT: 4. BETA-CAROTENE AND VITAMIN A LEVEL IN SERUM.

El-Aaser AA, El-Merzabani MM, Abdel-Reheem KA, Hamza BM
Natl. Cancer Inst., Kasr Aini St., Foum Kaleg, Cairo, Egypt
Tumori; 68(1):19-22 1982

The possible role of vitamin A in the pathogenesis of bilharzial bladder cancer among Egyptians, particularly as it relates to the histopathologic tumor type, was investigated. Bilharzial patients and bladder cancer patients with squamous cell carcinoma, the most prevalent type in Egypt, showed significantly lower levels of vitamin A than normal male subjects. In contrast, bladder cancer patients with transitional cell carcinoma had levels that were not significantly different from normal male subjects. The possible role of vitamin A in the etiology of bilharzial bladder cancer is discussed. (Author abstract) (22 Refs)

10. A STUDY ON THE ETIOLOGICAL FACTORS OF BILHARZIAL BLADDER CANCER IN EGYPT. 6. THE POSSIBLE ROLE OF URINARY BACTERIA.

El-Aaser AA, El-Merzabani MM, Higgy NA, El-Habet AE
Natl. Cancer Inst., Kasr Aini St., Foum Kaleg, Cairo, Egypt
Tumori; 68(1):23-28 1982

A correlation was obtained between a positive nitrite test in urine and the severity of urinary bacterial infection. Bacteria isolated from the urine of of bilharzial or bladder cancer patients were found to be rich in nitrate reductase activity. 'Escherichia coli' was the most common microorganism isolated from these specimens. Urine and several urinary constituents activate bacterial nitrate reductase. beta-Glucuronidase activity in the urine of patients with chronic 'Schistosoma hematobium' infection and bladder cancer was measured and shown to be significantly greater than that of urine of normal control subjects. Urinary bacterial infection was shown to be the source of the increased urinary level of enzyme activity at pH 7.0. (Author abstract) (26 Refs)

11. VARIATIONS IN CANCER MORTALITY AMONG LOCAL AUTHORITY AREAS IN ENGLAND AND WALES: RELATIONS WITH ENVIRONMENTAL FACTORS AND SEARCH FOR CAUSES.

Gardner MJ, Winter PD, Acheson ED
Medical Res. Council's Environmental Epidemiology Unit, Univ. Southampton, Southampton General Hosp., Southampton SO9 4XY, England
Br Med J; 284(6318):784-787 1982

Geographical variations in specific causes of mortality among the 1366 local authority areas of England and Wales as defined in 1971 were studied by examining extracts from death certificates held on computer tape. Five items of information on each death (yr of death, age at death, sex, local authority area of residence, and the underlying cause of death, during the 11 yr 1968-78) permitted a more detailed investigation than had been possible before. Analysis of some early results of the study (including maps of mortality for pleural mesothelioma, nasal cancer, and bladder cancer) suggested that, despite the known limitations of death certification, systematic study of the mortality of small areas may give clues to etiological factors in the environment. Analyses relating mortality to the distribution of environmental factors and examining disease profiles of each area may also provide clues. These will be followed up by other methods of study, such as case-control techniques. (Author abstract) (20 Refs)

12. FLUORIDATION AND CANCER: AN EPIDEMIOLOGIC APPRAISAL.

Neuberger JS
Dept. Community Health, Univ. Kansas Sch. Medicine-Kansas City, Kansas City, KS
J Kans Med Soc; 83(3):134-139 1982

The relationship of water fluoridation to cancer has been studied extensively, perhaps more intensively than many other chemicals in the environment. In 1977, a paper was published under the auspices of the National Health Foundation (NHF), showing a greater increase in the cancer death rates (1940-1970) in the 10 largest American cities that began fluoridation before 1960, as compared to the 10 largest cities not fluoridated as of 1969 (excluding New York City and Detroit). The studies done by the NHF have provided the anti-fluoridationists' greatest arguments against water fluoridation. However, these studies did not meet even minimally acceptable standards

for generally accepted epidemiologic research. Other studies by other scientific investigators (including several by the National Cancer Institute) indicate that fluoride is not even associated with cancer, still less a causative factor. The age-adjusted mortality rates in white Kansas residents (both sexes) for 1973-1977 were studied for cancer sites that might possibly be related to water borne carcinogens (stomach, colon, rectum, liver, pancreas, kidney, bladder, and bone), in fluoridated and nonfluoridated Kansas counties of the highest populations. (Wichita, the largest city in Kansas, is not fluoridated). The data were analyzed in terms of person-yr of exposure to fluoride. No association of artificial water fluoridation with cancer was found. It is concluded that current evidence does not support the contention that fluoride is associated with cancer. (9 Refs)

13. COFFEE, TEA AND CANCER: HOW TO TEST HYPOTHESES ON LIFESTYLE AND DISEASE?.

Olsson H, Brandt L
Onkologiska kliniken, Lund, Sweden
Lakartidningen; 79(4):196-197 1982

Coffee and tea consumption of 550 tumor patients was analyzed based on questionnaire data. The patients included 19 with seminomas, 36 with cancer of the upper part of the digestive tract (lips, oral cavity, epipharynx, hypopharynx and esophagus), 59 with Hodgkin's disease, 64 with tumors of the larynx and lungs, 36 with thyroid tumors, 120 with cancer of the urinary bladder or kidneys, 28 with skin cancer, 94 with breast cancer, 16 with testicular teratomas, 28 with melanomas, 20 with cancer of the lower parts of the digestive tract (stomach, bile ducts, pancreas, colon and rectum), and 18 with tumors of the paranasal sinuses, auditory meatus and parotid glands. The median coffee consumption of the patients was 3-5 cups/day, ie, approx the same as in the general population. Fifty-three per cent of the patients with seminomas, 50% of those with cancer of the upper part of the digestive tract and 47% of those with Hodgkin's disease consumed large amounts of coffee (5 cups/day or more). The median tea consumption of the patients was 0 cup/day. Forty-four per cent of the patients with testicular teratomas, 31% of those with thyroid tumors, 32% of those with seminomas, and 29% of those with Hodgkin's disease consumed large amounts of tea (2 cups/day or more). The findings indicate that hypotheses based on complex data on lifestyle (education, occupational status, living conditions, dietary and smoking habits, and alcohol consumption) should be tested in epidemiological studies, rather than the possible relationship between tea and coffee consumption, on one hand, and certain diseases, on the other hand. (6 Refs) (In SWE)

14. INCREASED ABNORMAL UROTHELIAL CELLS IN VOIDED URINE FOLLOWING EXCRETORY UROGRAPHY.

Fischer S, Nielsen ML, Clausen S, Vogelsang M, Hogsborg E
Dept. Pathology, Frederiksberg Hosp., DK-2000 Copenhagen, Denmark
Acta Cytol (Baltimore); 26(2):153-158 1982

A prospective study of 45 consecutive patients scheduled for excretory urography demonstrated a statistically significant increase in the proportion of abnormal urothelial cells, including pseudomalignant cells, recovered in the urine between 3 hours and 7 days after urography. The total number of urothelial cells recovered in the urine did not increase at any time. The Millipore filter imprint technique, which allows semiquantitative examination of urothelial cells from urine, is discussed. (Author abstract) (19 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

15. COMPARATIVE STUDIES OF NEOPLASTIC RESPONSE TO A SINGLE DOSE OF NITROSO COMPOUNDS. 7. THE EFFECT OF N-NITROSOBIS (2-HYDROXYPROPYL)AMINE IN SYRIAN GOLDEN HAMSTERS.

Pour PM, Salmasi SZ
Preclinical Res., Toxicology Dept., Sandoz AG, CH-4133 Pratteln 4, Switzerland
J Cancer Res Clin Oncol; 102(3):265-269 1982

Single sc applications of N-nitrosobis(2-hydroxypropyl)amine (BHP) caused carcinogenic effects in adult Syrian golden hamsters at doses as low as 1/40 of the LD50. The tumor spectrum decreased at lower doses, which affected the pancreas more strongly than the liver, whereas higher doses exhibited a more pronounced hepatocarcinogenicity and also induced tumors in the respiratory tract, gallbladder, kidney, and vagina. These results demonstrated a potent pancreatic carcinogenic effect of BHP at the lowest dose level. Hence, the presence of BHP in the environment, even in small quantities, should be regarded as a potential hazard to human health. (Author abstract) (9 Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

16. PERMISSIVE ROLE OF THE PITUITARY IN THE INDUCTION AND GROWTH OF ESTROGEN-DEPENDENT RENAL TUMORS.

Lin YC, Loring JM, Villee CA
(c/o Villee), Harvard Medical Sch., Boston, MA, 02115
Cancer Res; 42(3):1015-1019 1982

Prolonged administration of estrogen to hamsters by implanted pellets induces no t only renal adenocarcinomas but also enlarges pituitaries with hyperplastic and neoplastic changes, especially in the pars intermedia. The pituitaries of the diethylstilbestrol-implanted animals weigh 90 to 150 mg; those of control animals without diethylstilbestrol pellets weigh 7 to 12 mg. Castrated male hamsters were hypophysectomized, implanted with diethylstilbestrol pellets, fed laboratory chow ad libitum, and given 5% glucose in water to drink. New pellets were implanted every 3 mo, and the animals survived for 12 to 15 mo. At autopsy, none of the animals had a tumor. Sixty-two of 65 control castrated males with the same schedule of pellet implantation developed tumors. Hypophysectomized castrated males implanted with diethylstilbestrol pellets were given daily injections of 1 ug each of follicle-stimulating hormone, luteinizing hormone, and prolactin; or with 0.9% NaCl solution. These animals survived for 12 to 15 mo, but none developed kidney tumors. Other castrated males were hypophysectomized and implanted with diethylstilbestrol pellets, and 2 mo later tumor tissues were transplanted under the kidney capsule. Eighty days later, no tumors were evident in the kidneys of these animals. Control castrated males were implanted with diethylstilbestrol pellets, and 2 mo later tumor tissue was transplanted under the kidney capsule. Between 60 and 85 days later, 13 of the 15 controls had developed renal tumors. The concentrations of circulating follicle-stimulating hormone and

luteinizing hormone in animals with diethylstilbestrol implants decreased with time and, by 7 mo, were similar to those in hypophysectomized animals. The concentration of prolactin in animals with diethylstilbestrol pellets increased with time and reached twice the value in the control animals without diethylstilbestrol pellets. These studies suggest that some factor secreted by the pituitary may be involved as a promoter or a cocarcinogen in the estrogen induction of kidney tumors. (Author abstract) (19 Refs)

17. INHIBITION OF METHYLAZOXYMETHANOL-INDUCED INTESTINAL TUMORS IN THE RAT BY PYRAZOLE WITH PARADOXICAL EFFECTS ON SKIN AND KIDNEY.

Notman J, Tan QH, Zedeck MS
(c/o Zedeck), Memorial Sloan-Kettering Cancer Center, New York, NY, 10021
Cancer Res; 42(5):1774-1780 1982

Methylazoxymethanol is a potent carcinogen and induces tumors predominantly of the small intestine and colon following a single injection. Previous data indicated that alcohol dehydrogenase could convert this carcinogen to a reactive alkylating agent. Rats were treated with an inhibitor of this enzyme, pyrazole, 2 hr prior to their receiving the carcinogen. The development of intestinal and colonic tumors was prevented. The rats did, however, develop numerous tumors of the skin and kidney. Analyses of the complete autopsies are presented. The data indicate that intestinal and colonic alcohol dehydrogenase p lays a role in the tumorigenic effects of methylazoxymethanol and that other non-pyrazole-sensitive enzymes exist in other organs that can also activate this carcinogen. (Author abstract) (21 Refs)

18. THE SYNERGISTIC EFFECT OF AFLATOXIN B1 AND OCHRATOXIN A IN RATS.

Rati ER, Basappa SC, Sreenivasa Murthy V, Ramesh HP, Ramesh BS, Singh GB
Central Food Technological Res. Inst., Mysore, India
J Food Sci Tech; 18(5):176-179 1981

Male albino weanling Wistar rats were fed a daily 1/20 LD50 dose of aflatoxin B1 and/or ochratoxin A for 4 months with purified or natural diets. No tumors were found. No synergistic growth effects were seen on the natural diet, but adverse synergism was seen in weight gain and specific kidney weight on the purified diet. Histopathologic changes in liver and kidney are discussed. (25 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

19. PERSISTENCE OF DNA ADDUCTS IN RAT LIVER AND KIDNEY AFTER MULTIPLE DOSES OF THE CARCINOGEN N-HYDROXY-2-ACETYLAMINOFLUORENE.

Beland FA, Dooley KL, Jackson CD
Natl. Center Toxicological Res., Food and Drug Admin., Jefferson, AR, 72079
Cancer Res; 42(4):1348-1354 1982

Male and female Sprague-Dawley rats were treated by gastric intubation either 1, 2, 3, or 4 times at biweekly intervals with 10-mg/kg doses of the hepatocarcinogen N-[ring-3H]-hydroxy-2-acetylaminofluorene. Then either 1 or 14 days following the last treatment, the concentrations of 2-aminofluorene and 2-acetylaminofluorene adducts in liver and kidney DNA were established. 2-Acetylaminofluorene adducts were found in male rat liver DNA only. The C-8-acetylated adduct, N-(deoxyguanosin-8-yl)-2-acetylaminofluorene, was detected only on the day following treatment at a concentration between 1.0 and 2.4 pmol/mg DNA. A second acetylated adduct, 3-(deoxyguanosin-N2-yl)-2-acetylaminofluorene, was found at both 1 and 14 days after treatment and, as a result, increased in concentration with repeated doses, from 0.2 pmol/mg DNA after one dose to 2.8 pmol/mg DNA after four treatments. The major adduct detected in male rat liver and the only adduct found in female rat liver and in kidney from either sex was N-(deoxyguanosin-8-yl)-2-aminofluorene. This adduct was slowly lost from the DNA and therefore increased in concentration with repetitive treatments as follows: male liver, 4.0 to 9.4 pmol/mg DNA; female liver, 11.4 to 30.6 pmol/mg DNA; male kidney, 1.1 to 1.8 pmol/mg DNA; and female kidney, 1.8 to 17.7 pmol/mg DNA. These data indicate that certain DNA adducts can accumulate in both target and non-target tissues and therefore suggest that persistence of DNA adducts per se is not sufficient for tumor induction. (Author abstract) (64 Refs)

20. FORMATION AND REMOVAL OF (GUAN-8-YL)-DNA-2-ACETYLAMINOFLUORENE ADDUCTS IN LIVER AND KIDNEY OF MALE RATS GIVEN DIETARY 2-ACETYLAMINOFLUORENE.

Poirier MC, True B, Laishes BA
NIH, Building 37, Room 3A19, Bethesda, MD, 21205
Cancer Res; 42(4):1317-1321 1982

Radioimmunoassay has been used to measure acetylated and deacetylated deoxyguanosine C-8 DNA adducts of 2-acetylaminofluorene in liver and kidney DNA of male Wistar-Furth rats fed a dietary regimen of 0.02 or 0.04% 2-acetylaminofluorene. When adduct formation was monitored during continuous feeding up to 60 days, substantial levels of binding (80 fmol/ug DNA) were observed in liver by 1 day, and maximum steady-state values averaging 230 fmol/ug DNA were reached by 30 days. Initially, during the continuous feeding, about 80% of the total C-8 adducts were deacetylated [N-deoxyguanosin(8-yl)aminofluorene], and this proportion increased to about 97% by 15 and 30 days of administration of 0.04 and 0.02% 2-acetylaminofluorene diets, respectively. Levels of C-8 adducts bound to kidney DNA in the same animals averaged 10 to 15% of the liver values with greater than or equal to 80% of these adducts in the deacetylated form. In separate experiments, rats were exposed to 2-acetylaminofluorene for 3, 7, 28, and 112 days; the carcinogen-containing diet was discontinued; and C-8 adducts were monitored during 1, 7, and 28 days of feeding control diet. At both carcinogen doses, after dietary administration for 3 or 7 days, there was a rapid decrease in liver C-8 adducts so that, after 28 days on control diet, 65 to 90% of the original adducts were no longer present in the DNA. In contrast, in animals fed 0.02% 2-acetylaminofluorene for 28 days, there were high levels (70 to 100% of the original C-8 adduct) remaining on the DNA at the end of 28 days on control diet. This apparent loss in capacity for removal of C-8 adducts is discussed in relation to biological and biochemical changes induced in the rat liver during 2-acetylaminofluorene hepatocarcinogenesis. (Author abstract) (26 Refs)

21. A FREE RADICAL MECHANISM FOR ARYLAMINE INDUCED CARCINOGENESIS INVOLVING PEROXIDES.

Vasdev S, Tsuruta Y, O'Brien PJ
Dept. Biochemistry, Memorial Univ. Newfoundland, St John's, Newfoundland, Canada A1B 3X9
Biochem Pharmacol; 31(4):607-608 1982

A 1 e oxidation of N-methyl-4-aminoazobenzene (MAB) catalyzes more binding than the 2 e monooxygenase mechanism in the presence of liver sulfotransferase. Covalent binding of (14C)MAB metabolites to exogenous DNA or microsomal protein demonstrated that hydroperoxide was almost 400x more effective than NADPH in catalyzing the binding. NADPH/reductase may reduce the radical formed by the 1 e oxidation pathway of cytochrome P450. The hydroperoxide catalyzed binding was not affected by addition of cytosol, while the NADPH system was markedly enhanced. Addition of ATP and sulfate further enhanced the c ytosol effect, suggesting that the cytosol effect was probably due to sulfotransferase acting on the NOH MAB formed by the 2 e oxidation pathway carried out by microsomal amine oxidase/4. No NOH MAB was formed with hydroperoxide. Cytochrome P450 catalyzed both N demethylation and ring hydroxylation of MAB and the N hydroxylation was catalyzed by microsomal amine oxidase. In dogs and mice, the 1 e pathway of the monooxygenase activity of bladder and lung tissue may be responsible for carcinogenesis in these organs following administration of p-dimethylaminoazobenzene. In mouse liver carcinogenesis, both the 1 e and 2 e pathways should be considered. (9 Refs)

22. NUCLEAR CATALYZED ANTIBIOTIC FREE RADICAL FORMATION.

Bachur NR, Gee MV, Friedman RD
Lab. Clinical Biochemistry, Baltimore Cancer Res. Program, NCI, Baltimore, MD, 21201
Cancer Res; 42(3):1078-1081 1982

Nuclei isolated from rat liver, heart, and kidney catalyze oxygen consumption in the presence of reduced pyridine nucleotide (NADPH) and quinone or quinone-imine antibiotics such as adriamycin, daunorubicin, actinomycin D, mitomycin C, and streptonigrin. The Km and Vmax values for NADPH were 2.4 x 10(-3) M and 3 x 10(-8) mol O2 per min per mg protein and Km values for the antibiotics ranged from 1.4 x 10(-4) M to 5.9 x 10(-6) M. Metabolism of the anthracycline antibiotics, ie, reductive glycosidase reaction, occurs in reaction mixtures after all oxygen is consumed. During the reaction, free-radical species of Adriamycin and daunorubicin are detectable by electron paramagnetic resonance spectrometry. These observations indicate that some cytotoxic antibiotics can be activated to a free-radical state at the site where damage to nuclear DNA may result. (Author abstract) (23 Refs)

23. VARIATIONS OF GLYCOGEN LEVEL AND ALPHA-GLUCOSIDASE ACTIVITY IN HUMAN MALIGNANT EPITHELIAL CELL LINES IN CULTURE.

Paris H, Rousset M, Terrain B, Chevalier G, Zweibaum A, Murat JC
Institut de Physiologie, Universite Paul Sabatier, 31400 Toulouse, France
Int J Biochem; 14(2):141-145 1982

Variations of total protein and glycogen content and of alpha-glucosidase (AG) activities were determined during culture of five cell lines derived from human cancers: HRT-18, rectum; SW-839, kidney; MeWo, melanoma; SK-OV-3, ovary; and RT-4, urinary bladder. In HRT-18 cells, neutral (pH 7) AG was found mainly in the exponentially growing cells, while lysosomal (pH 4.5) AG was preferentially increased during the stationary phase. The lysosomal and neutral AG profiles were similar in all the cell lines, and parallel to the glycogen accumulation curves; activity was very low during the early stages of cell culture and then it increased gradually. Since highest neutral AG activity coincides with the phase of maximal cell proliferation, it is proposed that its activity can be related to an enhanced synthesis of glycosylated products. Many glucose units would be used for such an anabolic process, and hence would not be available for accumulation as a reserve polymer. (29 Refs)

24. DECREASE IN PROTEIN CONTENT AND CELL VOLUME OF CULTURED DOG KIDNEY EPITHELIAL CELLS DURING GROWTH. IMPORTANCE FOR TRANSPORT MEASUREMENTS.

Erlinger S, Saier MH
Unite de Recherches de Physiopathologie Hepatique (INSERM), Hopital Beaujon, F-92118 Clichy Cedex, France
In Vitro; 18(3):196-202 1982

Protein content per cell and cell volume of the canine kidney epithelial cell line, MDCK, and one of its chemically induced tumorigenic transformants (T1) were examined during growth in serum-containing and serum-free, hormonally defined media. Both protein content per cell and cell volume (measured with 3-O-methyl-D-glucose) decreased when cell density increased. Significant inverse linear correlations were found between protein content (and cell volume) and the log of the cell number. Equations relating these variables were derived. No difference was detected between cells grown in serum-containing and in serum-free media. Results of 22Na+ uptake experiments differed markedly when expressed as a function of cell number or as a function of protein content or cell volume. However, protein content and cell volume bore a constant relationship to one another, and expression of results as a function of protein content or cell volume yielded qualitatively similar results. These findings show that in MDCK cells, as in other cell lines, protein content and cell volume decrease markedly during growth and that these variations must be taken into account when expressing and interpreting the results of transport measurements. (Author abstract) (25 Refs)

25. NUCLEAR ANDROGEN RECEPTOR AS MARKER OF RESPONSIVENESS TO MEDROXYPROGESTERONE ACETATE IN HUMAN RENAL CELL CARCINOMA.

Concolino G, Marocchi A, Toscano V, Di Silverio F
Istituto di Clinica Medica Generale e Terapia Medica V, Universita di Roma, Roma, Italy
J Steroid Biochem; 15:397-402 1981

Androgen receptors (AR) were measured in the cytoplasmic and nuclear fractions of human renal cell carcinoma (RCC) in order to find a parameter (ARn) which could better predict the response to hormonal therapy. Cytosol AR were detected in 50% and ARn in 57% of the tumors examined. AR do not only help to define the hormone-dependent human RCC, but may also be useful in the selection of patients to be treated with medroxyprogesterone acetate (MPCA). MPCA could counteract the promoting action of estrogens on tumor growth only in patients with ARn positive tumor. (27 Refs)

26. AMYLOID A IN SYSTEMIC AMYLOIDOSIS ASSOCIATED WITH CANCER.

Husby G, Marhaug G, Sletten K
Dept. Rheumatology, Inst. Clinical Medicine, Univ. Tromso, Tromso, Norway
Cancer Res; 42(4):1600-1603 1982

Amyloid fibrils from two cases of cancer-associated, systemic amyloidosis with renal cell carcinoma and mesothelioma as the respective underlying disorders were studied. The immunochemical studies suggested strongly that amyloid A comprised a principal fibril component in both cases of cancer-associated amyloidosis. This was definitely proven by amino acid sequence analyses, which revealed structural homology between a purified subcomponent of the amyloid fibrils from both of the two cases of cancer-associated amyloidosis and previously sequenced amyloid A proteins. The chemical composition of the amyloid fibrils from systemic amyloidosis associated with cancer thus corresponded to that seen in amyloidosis reactive to inflammatory diseases and Hodgkin's disease. Amyloid proteins of immunoglobulin light chain type, which are found associated with myelomatosis, macroglobulinemia, and idiopathic (primary) amyloidosis, were not found in the two amyloid preparations. Renal cell carcinoma appears to be an effective stimulator of amyloid formation, while only one case of amyloidosis associated with mesothelioma has been reported previously. (Author abstract) (33 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

27. EFFECT OF 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN AND PHENOBARBITAL ON THE OCCURRENCE AND DISTRIBUTION OF FOUR CYTOCHROME P-450 ISOZYMES IN RABBIT KIDNEY, LUNG, AND LIVER.

Dees JH, Masters BS, Muller-Eberhard U, Johnson EF
Dept. Biochemistry, Univ. Texas Health Science Center at Dallas, Dallas, TX, 75235
Cancer Res; 42(4):1423-1432 1982

The effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and of phenobarbital (PB) on the distribution and occurrence of four cytochrome P-450 isozymes, Forms 2, 3, 4, and 6, in the kidney, lung, and liver of adult male rabbits was investigated using immunofluorescence. In the kidney, Forms 2 and 3 were localized in the proximal tubules of both untreated and PB-treated animals, while antibodies to Forms 4 and 6 showed weak to negative staining. In TCDD-pretreated animals, Forms 4 and 6 appeared in the renal endothelium, in addition to staining the proximal tubular epithelium intensely. Form 2 was the only isoenzyme of those studied found to be present in the lungs of normal and PB-treated rabbits; it was also present in lungs of TCDD-pretreated rabbits. Form 3 was not detected in any of the rabbit lungs examined. Forms 4 and 6, while not apparent in the lungs of normal or PB-treated animals, were found in the lungs of TCDD-treated animals and also appeared in the endothelium of the pulmonary arteries and veins. All forms tested were present in control liver. The staining for Form 2 was intense in the livers of PB-pretreated animals, as was the staining for Forms 4 and 6 in the livers of TCDD-pretreated animals. Our results indicate that, while PB al tered the intensity of staining for Form 2 in the liver and kidney, TCDD altered both the staining intensity and distribution of the isozymes in kidney, lung, and liver, producing, for example, a localization of Forms 4 and 6 in the endothelium of both the kidney and lung which was not seen in either untreated or PB-pretreated rabbits. (Author abstract) (48 Refs)

28. CYTOCHEMICAL MARKERS OF BLADDER CARCINOGENESIS.

Wilson PD, Summerhayes IC, Hodges GM, Trejdosiewicz LK, Nathrath WJ
Physiologisches Institut der Universitat Munchen, Pettenkoferstrasse 12, 8 Munchen 2, W. Germany
Histochem J; 13(6):989-1007 1981

Enzyme cytochemical and immunocytochemical techniques were used at the light and electron microscope levels to study the distribution of potential enzyme and antigen markers of chemical transformation in rat and mouse bladders. In in vivo methylnitrosourea-induced rat tumors, alkaline phosphatase (AP) localization was normal on the external surface of the plasma membranes of some cells whereas in others AP was detected only on intracellular membranes. 5'-Nucleotidase (5NU) localization was abnormal in all cells, being seen on endoplasmic reticulum and nuclear membranes only, while in normal bladders only ectoenzyme localization was seen. After tumors were cultured as explants for 15 days, heterogeneity of AP and 5NU localization was seen on the plasma membranes. Enzyme production within some cells was variable while in other cells, only parts of the membrane reacted heavily. A bimodal pattern of AP localization was seen in transformed cell cultures and tumors of mouse bladder derived by in vitro treatment of explants with dimethylbenz(a)anthracene. Cells had either normal ectoenzyme reaction product or abnormal intracellular membrane reaction product. 5NU and adenosine diphosphatase were lost and an Mg.ATPase and a cyclic AMP-independent, calcium-insensitive 'protein phosphatase' were induced in transformed cell cultures. Immunocytochemical study revealed an epithelial antigen in the cytoplasm of both normal and transformed cells which was associated with reticular cytoplasmic ground substance, plasma membrane vesicles and cytoskeletal elements. (29 Refs)

29. DNA PROFILE AND TUMOUR PROGRESSION IN PATIENTS WITH SUPERFICIAL BLADDER TUMOURS.

Gustafson H, Tribukait B, Esposti P
Dept. Urology, Karolinska Hosp., Stockholm, Sweden
Urol Res; 10(1):13-18 1982

Two hundred-twenty nine cases of surgically treated superficial bladder tumors Grade 1-2, category Ta or T1, were followed clinically and by flow cytofluorometry (FCM). The mean follow-up time for continuous FCM was 2.6 yr. Three different types of DNA pattern were found in Grade 2 tumors: diploid DNA pattern; tetraploid DNA pattern; and non-tetraploid types with hypo- and hypertetraploid patterns. O ne hundred-seventy five cases were diploid and 54 were aneuploid. Tumor progression was not seen in the 175 cases with repeatedly diploid DNA pattern. In the cases with tumor progression, the degree of ploidy could be related to the frequency of progression: 50% of the cases with triploid-hypotetraploid DNA pattern showed progression, while 10% with tetraploid DNA showed progression. FCM analysis in 33 cases of recurring tumors revealed that the degree of ploidy and the proportion of S-phase cells was fairly constant. The results indicate that the DNA profile can characterize a bladder tumor by its degree of ploidy and proliferation, and may be significant in

predicting progression in cases of well and moderately well differentiated superficial bladder carcinoma. (11 Refs)

30. CHARACTERIZATION OF BLADDER PAPILLOMA BY TWO-PARAMETER DNA-RNA FLOW CYTOMETRY.

Klein FA, Melamed MR, Whitmore WF, Herr HW, Sogani PC, Darzynkiewicz Z

Urology Service Dept. Surgery, Memorial Sloan Kettering Cancer Center, Cornell Univ. Medical Coll., New York, NY, 10021

Cancer Res; 42(3):1094-1097 1982

Two-parameter flow cytometry (FCM) studies of 0.9% NaCl solution bladder irrigation specimens were performed on 48 patients with histologically orderly or atypical papilloma of the urinary bladder in order to assess the value of RNA as a possible second parameter, along with DNA, in the detection of bladder tumors. DNA, RNA, and nuclear diameter measurements were obtained for each of 5,000 cells/sample, and analyses were based on the distributions of those values. With the use of DNA content alone, 22 cases (46%) were classified positive by FCM. With RNA content as an additional parameter, 40 cases (83%) were positive. Two cases were suspicious, and six cases were normal by both parameters. Of 28 patients with papillomas showing histological atypia, 16 patients had positive DNA histograms, including 3 patients with aneuploid stemlines, but 24 of the 28 patients had positive RNA histograms. Of 20 patients with orderly papillomas, 6 patients had positive DNA histograms, including 3 patients with aneuploid DNA stem cell lines, but 16 of the 20 patients had positive RNA histograms. Thus, the probability of positive DNA histograms is higher in atypical papillomas (57%) than in orderly papillomas (30%), whereas elevated (positive) RNA is more characteristic of all papillomas without distinction between those that are histologically atypical (86% positive) or orderly (80% positive). For patients at risk of developing papillary bladder tumors, two-parameter DNA-RNA FCM appears to offer greater diagnostic sensitivity than does FCM based on DNA content alone. (Author abstract) (16 Refs)

31. BIOLOGICAL CHARACTERISTICS AND VIRAL SUSCEPTIBILITY OF A STABLE DOG KIDNEY CELL LINE.

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Life Sciences Div., SRI International, Menlo Park, CA, 94025

In Vitro; 18(3):220-226 1982

A cell line derived in 1956 from normal dog kidney is described. The cells are epithelial, contact-inhibited, and can be maintained in the same culture vessels for periods of more than 2.5 yr. Karyologically, the cells are hypodiploid with a modal number of 72 as opposed to the diploid number of 78. The karyotype indicates male origin of the cells and clonal derivation of extant cultures due to the presence of two marker chromosomes in all metaphases observed. At the 159th passage the dog kidney (DK) cells did not produce tumors in athymic rats. At least 13 viruses of various types produced transmissible cytopathogenic effects in the DK cells, including all of the human influenza viruses investigated. (Author abstract) (23 Refs)

32. BEHAVIOR OF PRIMARY AND SERIALLY TRANSPLANTED ESTROGEN-DEPENDENT RENAL CARCINOMA CELLS IN MONOLAYER AND IN COLLAGEN GEL CULTURE.

Talley DJ, Roy WA, Li JJ

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In Vitro; 18(2):149-156 1982

When estrogen is present in culture medium, enzyme-dissociated cells from estrogen-induced primary renal tumors in Syrian hamsters and from 1st to 4th serially transplanted carcinomas in monolayer culture contain progesterone receptor levels that are similar and comparable to those in tumors in vivo (ie, 2 pmol/3 x 10(6) cells). Despite the similarity of receptor levels in cultured cells isolated from primary and transplanted tumors, the ability of cells to be maintained in culture differs considerably from one tumor stage to another. When cultured as monolayers in plastic flasks, isolated cells from primary tumors exhibit a marked decline in cell number after 4 to 6 days in culture. On the other hand, monolayer-cultured cells from first and second transplantation tumors remain essentially constant in cell number over a 2 wk culture period and cells from third transplantation tumors undergo a two- to threefold increase in cell number during 2 wk in culture. When primary tumor cells are cultured in collagen gels, the decline in cell number over a 2 wk culture period is prevented and progesterone receptor levels remain elevated. Cells cultured from first transplantation tumors exhibit a delayed decline in cell number beginning after 2 wk in monolayer culture. The decline in cell number in monolayer culture, like that for cells from primary tumors, can be prevented by culturing cells from first transplantation tumors in collagen gels. Neither cells from primary nor first transplantation tumors exhibit significant increases in cell number in collagen gels. Increasing the serum concentration of growth medium to 30% does not stimulate growth of cells under these conditions. Cells isolated from fourth transplantation tumors undergo a fourfold increase in cell number over a 1 mo culture period whether cells are cultured as monolayers or in collagen gels. (Author abstract) (23 Refs)

33. ESTABLISHMENT OF A HUMAN RENAL PELVIC CANCER CELL LINE PRODUCING TISSUE THROMBOPLASTIN AND PLASMINOGEN ACTIVATOR.

Naito S, Tanaka K, Kanamori T, Hisano S, Momose S

Dept. Pathology, Faculty Medicine, Kyushu Univ., Fukuoka, Japan

Urol Res; 10(1):19-25 1982

A human renal pelvic cancer cell line, KP 1, has been established and subcultured 190 times over a 5 yr and 9 mo period. The cells, which have a doubling time of 35 hr, produced subcutaneous tumors in BALB/c nude mice at the 7th and 135th passages, the tumors exhibiting histological appearances similar to the original tumor. Chromosome analysis at the 53rd and 110th passages showed 100% aneuploidy with a model chromosome number in the hypertriploid range. KP 1 cells had both thromboplastic and fibrinolytic activities. Coagulation studies using Factor VII deficient and Factor IX deficient human plasma indicated that the thromboplastic activity is due to tissue thromboplastin of the tumor cells themselves. Fibrinolysis neutralization experiments with anti-urokinase IgG indicated that the plasminogen activator of KP 1 was immunologically identical to urokinase, the plasminogen activator in urine. As fibrin deposition is considered to be an important factor influencing growth and spread of tumor tissue, the KP 1 line should be a useful model system for studying the significance

of the coagulation-fibrinolysis system in human cancer. (24 Refs)

34. TISSUE CULTURE STUDIES IN THE UROLOGICAL FIELD, PARTICULARLY IN A RELATION TO THE FIBRINOLYTIC SYSTEM IN CANCER AND ITS CLINICAL IMPLICATIONS.

Hisazumi H, Misaki T, Naito K, Taya T, Uchibayashi T, Tsukahara K, Kobayashi T, Nakagima K, Kato M, Saitoh Y, Koizumi H, Nishino A, Koshida K
Dept. Urology, Sch. Medicine, Kanazawa Univ., Kanazawa, Japan
Hinyokika Kiyo; 27(7):829-841 1981

The results of tissue culture studies of urological cancers were presented in this special lecture. The tissue cultures have been introduced into our experimental investigations of the fibrinolytic system in neoplasms, particularly bladder cancer, and of an in vitro sensitivity test of anticancer drugs. In addition, the results of our clinically significant studies related to the fibrinolytic system in the diagnostic and therapeutic aspects of bladder cancer were reported. (22 Refs) (In JPN)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

35. LESS MEMBRANE-ASSOCIATED ACTIN IN TRANSFORMED VERSUS NORMAL RAT KIDNEY CELLS.

Rubin RW, Suchard SJ, Ozores JN
Dept. Anatomy, Univ. Miami Sch. Medicine, Miami, FL, 33101
Cell Biol Int Rep; 6(2):177-187 1982

The amount of membrane-associated (MA) actin was compared in normal rat kidney (NRK) cells and their Kirsten viral transformants (442 cells). Entrapment of non-specific proteins and/or chemically induced alterations of plasma membrane incurred during isolation were overcome by employing an isolation procedure which does not require gradient purification, sonication, or the use of chemical membrane stabilizers or detergents. Plasma membranes were isolated by adhering NRK and 442 cells to a poly-L-lysine treated surface, and lysing them with hypotonic buffer. Results showed that MA actin to total MA protein ratio is significantly greater for NRK than for 442 cells. (24 Refs)

36. TRANSFORMATION-DEPENDENT LOSS OF THE HYALURONATE-CONTAINING COATS OF CULTURED CELLS.

Underhill CB, Toole BP
Dept. Anatomy, Georgetown Univ. Sch. Medicine, 3900 Reservoir Road, Washington, DC, 20007
J Cell Physiol; 110(2):123-128 1982

Coats of a variety of cell types, including a rat fibrosarcoma (RFS) cell line which is known to synthesize large amounts of hyaluronate, and two sets of parent and virus-transformed cell lines [Swiss 3T3 vs Simian virus-3T3 cells and baby hamster kidney cells (BHK) vs polyoma-BHK] were studied. Cell coat size was determined by comparing the pattern of settled RBC on control cultures with that of streptomyces hyaluronidase-treated cultures. The cell coat of RFS cells was quite large, as much as 25 um thick in places. The coats of 3T3 and BHK cells were also readily apparent although somewhat smaller than that of RFS cells. In virus-transformed cells, the coats were either greatly reduced or absent. RFS cells had the largest amount of hyaluronate followed in order by the 3T3 and the BHK cells. The two virus-transformed cell lines had much less hyaluronate than their parental counterparts. Differences between the amounts of hyaluronate were also reflected in the amounts of hyaluronate secreted into the medium. Cell lines with large coats tended to retain a greater fraction of total hyaluronate at their surfaces. In chemical studies of cells grown in the presence of 3H-glucosamime, the specific activity of the hyaluronate varied considerably from cell line to cell line, with the highest values being obtained from virus-transformed cells. The results indicated that, at least in the case of 3H-glucosamine, incorporation of radioactivity is not a reliable index of the net production of hyaluronate. It was concluded that virus transformation leads to a decrease in the size of the hyaluronate coat of 3T3 and BHK cells. (33 Refs)

37. BIOCHEMICAL CHARACTERIZATION AND CELLULAR DISTRIBUTION OF A POLYMORPHIC, MURINE CELL-SURFACE GLYCOPROTEIN EXPRESSED ON LYMPHOID TISSUES.

Trowbridge IS, Lesley J, Schulte R, Hyman R, Trotter J
Dept. Cancer Biology, Salk Inst., Post Office Box 85800, San Diego, CA, 92138
Immunogenetics; 15(3):299-312 1982

A murine leukocyte surface glycoprotein (Mr = 95,000) has been defined by means of xenogeneic monoclonal antibodies. In normal hematopoietic tissues, the glycoprotein is found in highest amounts in the bone marrow. Flow cytometric analysis shows that essentially all bone-marrow cells express the glycoprotein and that it is a major component of a subpopulation of cells containing predominantly granulocytic precursors. In contrast, only about 5% of thymocytes express sufficient glycoprotein to be detected by flow cytometric analysis, although under stringent conditions up to 20% of thymocytes are susceptible to complement-mediated cytotoxicity using a monoclonal antibody against the glycoprotein. Functional assays showed that both prothymocytes and colony forming unit-spleen express the glycoprotein which is broadly distributed on murine hematopoietic tumor cell lines. However, although some Thy-1+ (T) cell lymphomas express large amounts of the glycoprotein, others do not express detectable quantities of the molecule. The glycoprotein is not restricted to hematopoietic cells and can be detected on lung, kidney, brain, and liver as well as cultured fibroblasts. Monoclonal antibodies against the glycoprotein cross-react with an antigen present on human cells. As described in the accompanying paper, the glycoprotein exists in two antithetical allelic forms and we show that it is identical to a polymorphic surface molecule independently characterized by Colombatti and co-workers. (Author abstract) (41 Refs)

38. IMMUNOLOGICAL DETECTION OF SPHINGOMYELIN-CARRYING PROTEIN IN TUMORS AND IN EMBRYONAL RAT LIVER.

Diatlovitskaia EV, Sinitsyna EV, Timofeeva NG, Iakimenko EF, Kuprina NI, Bergel'son LD
M. M. Shemiakin Inst. Bioorganic Chemistry, Moscow, USSR
Biokhimiia; 47(1):62-65 1982

The presence of sphingomyelin-carrying protein (SCP) was studied in the cytosol of hepatoma 27, sarcoma 45, Jensen sarcoma, nephroma RA, and in the normal, regenerating, and embryonal rat liver. SCP was assayed by double immunodiffusion technic. SCP was detected in the postmicrosomal supernatant of all tumors tested. SCP was also present in the embryonal

liver. SCP was not detected in the normal and regenerating liver, or in the blood of tumor-bearing rats. (16 Refs) (In RUS)

39. INCREASED INCIDENCE OF ANTIBODY IN PRE-MALIGNANT OCCUPATIONAL BLADDER CANCER.

Kumar S, Wilson PB, Costello CB
Christie Hosp. and Holt Radium Inst., Manchester M20 9BX, England
Oncology; 39(2):65-71 1982

Sera from 26.7% of the clinically healthy chemical workers with occupational exposure to bladder carcinogens produced immunofluorescent staining of the intracellular antigens of an allogeneic transitional cell carcinoma of the bladder. The incidence of positives among normal donor's and ea rly stage bladder cancer patients was much lower, viz. 3.6 and 6.7%, respectively. The same sera were also tested for their staining reactions against surface antigens of bladder tumor cells. Again sera from a higher proportion of chemical workers (28.6%) was found to produce immunofluorescence compared with normal donors (12.6%) and bladder cancer patients (18.6%). The elevated incidence of antibodies among chemical workers' sera was not due to autoantibodies which were similarly distributed in the three groups. Furthermore, the staining of chemical workers' sera was not tumor type specific as all the sera which stained membrane or intracellular components were found to lose their staining ability on absorption with non-bladder tumor cells. It is proposed that thes antibodies result from carcinogenic damage and have a physiological role to play. (Author abstract) (34 Refs)

40. DISTRIBUTION OF ABH ANTIGENS IN TUMORS OF THE BLADDER. A RETROSPECTIVE IMMUNOFLUORESCENCE STUDY.

Rouger P, Vallancien G, Leclerc JP, Gane P, Salmon C
Centre National de Referene pour les Groupes Sanguins, U76, CNTS, INSERM, 53 boulevard Diderot, F 75012 Paris, France
Nouv Presse Med; 11(6):419-421 1982

ABH antigens are normally present on the surface of the healthy urinary epithelium. In a significant number of patients with tumor of the bladder the epithelium loses these antigens. The loss appears to be unrelated to the grade or stage of the tumor, but the prognosis seems to be brighter when the ABH antigens are retained. (Author abstract) (16 Refs) (In FRE)

REVIEWS AND OTHER RELATED STUDIES

41. GROWTH AND DIFFERENTIATED PROPERTIES OF A KIDNEY EPITHELIAL CELL LINE (MDCK).

Saier MH
Dept. Biology, John Muir Coll., Univ. California San Diego, La Jolla, CA, 92093
Am J Physiol; 240(3):C106-C109 1981

Physiologic, biochemical, genetic, nd electron-microscopic findings in regulation of Madin-Darby canine kidney (MDCK) epithelial cell function are reviewed. Growth regulatory properties, growth in hormonally defined serum-free medium, isolation and properties of virally and chemically transformed variants of MDCK cells, differentiated properties of MDCK cells in vitro, and sodium ion transport systems in MDCK cells are discussed. (18 Refs)

42. CURRENT CANCER RESEARCH ON PEDIATRIC NEOPLASMS (SPECIAL LISTING).

International Cancer Research Data Bank Program Office
NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Pediatric Neoplasms (Special Listing) This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-929411:; 52pp. 1981

Special Listings of Current Cancer Research Projects are a service of the International Cancer Research Data Bank (ICRDB) program of the National Cancer Institute. Each listing contains des criptions of ongoing projects in one selected cancer research area. The descriptions are provided by cancer scientists in about 50 different countries. Etiological and epidemiological studies of pediatric neoplasms are discussed with respect to familial, genetic and congenital factors and the incidence of childhood cancer; in utero exposure to exogenous estrogens and other agents and the incidence of childhood cancer; iatrogenic exposure to radiation and drugs and the incidence of childhood cancer; demographic and other etiologic factors and the incidence of pediatric leukemia, lymphoma, nephroblastoma, and other solid tumors; and other environmental and etiologic factors. Preclinical chemotherapy studies in model systems of pediatric neoplasms are desribed. Clinical diagnosis and prognostic factors in childhood cancer are discussed. Therapy of leukemia, lymphoma, histiocytosis, intracranial tumors, neuroblastoma, nephroblastoma, retinoblastoma, rhabdomyosarcoma, and other solid tumors is outlined and pharmacokinetics, therapeutic complications, and patient supportive care are discussed. Clinical studies by cooperative groups, broad clinical programs, and educational programs are reviewed.

43. INDUSTRIAL BLADDER CANCER.

Glashan RW
Consultant Urologist, Royal Infirmary, Huddersfield HD3 3EA, England
Br Med J; 284(6316):614-615 1982

Incidence, history, industrial screening, and compensation for occupational bladder cancer are discussed. Past research indicated that exposure to benzidine, beta- or alpha- napthylamine increased the risk of dying from bladder cancer. Regular screening of workers is recommended since reversal of early cases is possible with intravesical doxorubicin therapy. Legislation to compensate workers who develop bladder cancer should be revised to include compensation for early disease, since carcinoma in situ usually occurs before the actual development of a tumor, and to include more people. (17 Refs)

44. METALS (SIDE EFFECTS).

Reinicke C
Dept. Pharmacology and Toxicology, Friedrich-Schiller Univ., Bachstrasse 18, 69 Jena, E. Germany
Side Eff Drugs Annu; (5):232-243 1981

Side effects of medically used metals and metal compounds are reviewed. Compounds discussed include aluminum, arsenic, bismuth, copper in intrauterine devices, gallium, gold, iron, mercury, selenium, silver, zinc, and metal in implants and prostheses. Particular attention is given to gold and histocompatibility antigens, and reactions in the kidney, liver, lung, and blood. Iron is discussed with respect to use in elderly patients, poisoning, and parenteral administration. (94 Refs)

45. CAUSES OF LEUKEMIAS AND CANCER: RECENT PROGRESS.

Bernard J
bd. de Perolles 53, 1700 Fribourg, Switzerland
Rev Med Suisse Romande; 102(1):95-103 1982

Roles of viruses, radiation, and toxic chemical substances in the development of cancer are discussed. Burkitt's lymphoma (BL), a B-cell lymphoma predominantly localized in facial bones and found most frequently in certain areas of Africa, was one of the first cancers to be related to a virus, Epstein Barr virus (EBV). EBV virus and its antibodies are found in BL patients. EBV virus, the infective agent in mononucleosis, has been shown to cause BL in marmosets. BL shows high correlations with geographic areas with levels of malaria, with chromosome translocation 8:14, and with lower socioeconomic groups. Viruses have also been implicated in cervix cancer (herpes virus), liver cancer (hepatitis B), and Hodgkin's disease. Evidence of radiation-induced cancers has been gained from studies of physicians, radiologists, and scientists exposed to radiation and of Hiroshima survivors. The relationship between radiation and cancer development is significant but varies among individuals. Dietary factors, such as tobacco (lung, bladder, and digestive cancers), alcohol (cirrhosis and liver cancer), and diet in general (high lipid diet and breast cancer) have been related to increased incidences of cancer. Leukemia has been observed in Hodgkin's disease patients treated with chemotherapy. A high incidence of lymphomas has been noted in patients who have undergone organ transplants. The role of heredity and geography in the etiology of cancer is discussed. (no Refs) (In FRE)

46. PLASMINOGEN ACTIVATORS IN NEOPLASTIC CELLS.

Goloborod'ko OP, Veremeenko KN
A. I. Kolomiichenko Res. Inst. Otolaryngology, Kiev, USSR
Eksp Onkol; 4(1):3-7 1982

Role of specific fibrinolytic enzymes in carcinogenesis is reviewed. Invasiveness and metastatic spreading of malignant cells was shown to be associated with plasminogen activators (PA). Progressive increase of fibrinolytic activity in the culture medium of transformed cells is due to elevated secretion of PA. The rate of PA formation and the degree of fibrinolytic activity are correlated with the morphological criteria of malignant transformation. Elevated secretion of PA was also observed in cultured cells of human malignant tumors (giant cell lung cancer, brain cancer, ovarian cancer). Long-term cultures of malignant cells showed gradual loss of ability to secrete PA. Increased PA levels were observed in the patients with cancer of the brain, breast, stomach, endometrium, cervix uteri, and bladder. PA was detected in the nuclear and mitochondrial fractions of murine Ehrlich's ascites carcinoma cells. The mechanism of PA effect was shown to be associated with the changes of the properties of cell membranes and membrane enzymes. (55 Refs) (In RUS)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO MAN. SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.
Schmahl D
International Agency for Cancer Research, Lyon, France
IARC Mongr Eval Carcinog Risk Chem Hum 26: 411 pp., 1981.

2. BIOCHEMICAL TOXICOLOGY OF BENZENE.
Snyder R, Longacre SL, Witmer CM, Kocsis JJ, Andrews LS, Lee EW
Dept. Pharmacology, Thomas Jefferson Univ., Philadelphia, PA, 19107
Rev Biochem Toxicol; 3:123-153 1981

3. A REVIEW OF THE MUTAGENICITY OF CHROMIUM.
Hatherill JR
Toxicology, Sch. Public Health, Univ. Michigan, Ann Arbor, MI, 48109
Drug Chem Toxicol; 4(3):185-195 1981

4. HORMONES AND BREAST CANCER.
Pike MC, Siiteri PK, Welsch CW
Dept. Family and Preventive Medicine, Univ. Southern California Sch. Medicine, Los Angeles, CA, 90033
Banbury Rep 8: 491 pp., 1981.

5. ORAL CONTRACEPTIVES: VOLUME 5.
Briggs MH, Briggs M
Deakin Univ., Geelong 3217, Australia
Oral Contraceptives: Volume 5. St. Albans, VT, Eden Medical Research Inc., Annual Research Reviews--Endocrinology, 331 pp., 1981.

6. EPIDEMIOLOGICAL STUDIES OF THE ROLE OF EXOGENOUS ESTROGENS IN THE ETIOLOGY OF BREAST CANCER.
Kelsey JL, Bulbrook RD, Korenman SG, Siiteri PK, Henderson BE
Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, New Haven, CT, 06510
Banbury Rep; 8:215-228 1981

7. EFFECTS OF LONG-TERM EXPOSURE TO LOW LEVELS OF OZONE: A REVIEW.
Melton CE
Civil Aeromedical Inst., Federal Aviation Admin., Oklahoma City, OK, 73125
Aviat Space Environ Med; 53(2):105-111 1982

8. METABOLIC INTERACTIONS OF HYDROCARBONS WITH MAMMALIAN LUNG.
Smith BR, Bend JR
Lab. Pharmacology, Natl. Inst. Environmental Health Sciences, NIH, Research Triangle Park, NC, 27709
Rev Biochem Toxicol; 3:77-122 1981

9. REVIEW OF EXPERIMENTAL CARCINOGENESIS BY COMPOUNDS RELATED TO VINYL CHLORIDE.
Chu KC, Milman HA
NCI, Bethesda, MD, 20205
Environ Health Perspect; 41:211-220 1981

10. REVIEWS IN BIOCHEMICAL TOXICOLOGY.
Hodgson E, Bend JR, Philpot RM
North Carolina State Univ., Raleigh, NC
Rev Biochem Toxicol 3: 368 pp., 1981.

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11. ALCOHOL AND CANCER.
MacSween RN
Univ. Dept. Pathology, Western Infirmary, Glasgow, Scotland
Br Med Bull; 38(1):31-33 1982

12. THE TOXICOLOGY OF COCOA AND METHYLXANTHINES: A REVIEW OF THE LITERATURE.
Tarka SM
Life Sciences, Hershey Foods Corp., Corporate Technical Center, Hershey, PA
CRC Crit Rev Toxicol; 9(4):275-312 1982

13. IMPLICATIONS OF DIETARY FIBER BREAKDOWN IN THE HUMAN COLON.
Cummings JH, Stephen AM, Branch WJ
MRC Dunn Clinical Nutrition Centre, Old Addenbrookes Hosp., Cambridge, CB2 IQE, England
Banbury Rep; 7:71-81 1981

14. BILE SALTS AND OTHER CONSTITUENTS OF THE COLON AS TUMOR PROMOTERS.
Reddy BS, Tannenbaum SR, Montesano R, Correa P, Haenszel W, Wattenberg LW
Div. Nutrition, American Health Foundation, Naylor Dana Inst. for Disease Prevention, Valhalla, NY, 10595
Banbury Rep; 7:345-363 1981

15. MOLD PRODUCING CARCINOGENIC TOXINS IN FOOD PRODUCTS.
Preda N
Institutul de medicina si farmacie, Cluj-Napoca, Romania
Rev Chir [Oncol]; 20(1):1-9 1981
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16. THE MEANING OF CANCER 'DIETS'.
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Abt. f. Onkologie-Hamatologie, Medizinische Klinik C, CH-9007 St. Gallen, Switzerland
MMW; 124(2):26-28 1982
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17. RISK FACTORS FOR CERVICAL CANCER.
Hulka BS
Dept. Epidemiology, Rosenau Hall 201H, Univ. North Carolina, Chapel Hill, North Carolina, NC, 27514
J Chronic Dis; 35(1):3-11 1982

18. EPIDEMIOLOGY OF THE MOST FREQUENTLY OCCURRING TUMORS OF THE DIGESTIVE SYSTEM.
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Abteilung Innere Medizin I, Universitatsklinik, Otfried-Muller-Strasse 10, D-7400 Tubingen, W. Germany
Internist (Berlin); 23(1):1-9 1982
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19. BLADDER CANCER.
Skrabanek P, Walsh A
Endocrine Oncology Unit, Mater Misericordiae Hosp., Dublin, Ireland
UICC Tech Rep Ser 60: 192 pp., 1981.

20. RECENT ADVANCES IN CANCER CYTOGENETICS.
Pogosiants EE
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Genetika; 17(12):2087-2099 1981
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21. CURRENT STATUS OF CYTOGENETIC STUDIES IN ANIMAL TUMORS WITH SPECIAL REFERENCE TO NONRANDOM CHROMOSOME CHANGES.
Sasaki M
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Cancer Genet Cytogenet; 5(2):153-172 1982

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22. ASBESTOS-RELATED DISEASES.
Casey KR, Rom WN, Moatamed F
Building 512, RMCOEH, Univ. Utah Medical Center, Salt Lake City, UT, 84112
Clin Chest Med; 2(2):179-202 1981

23. NONASBESTOS FIBROUS MINERALS.
Lockey JE
Building 512, RMCOEH, Univ. Utah Medical Center, Salt Lake City, UT, 84112
Clin Chest Med; 2(2):203-218 1981

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Apfeldorf R, Infante PF
Office Carcinogen Identification and Classification, Health Standards, Programs, Occupational Safety and Health Admin. U. S. Dept. Labor, Washington, DC, 20210
Environ Health Perspect; 41:221-226 1981

25. CONCEPTS IN CAUSALITY: CHEMICALLY INDUCED HUMAN URINARY BLADDER CANCER.
Lower GM
Center Human Systems, Inst. Environmental Studies, Univ. Wisconsin. WARF Building, 610 Walnut St., Madison, WI, 53706
Cancer; 49(5):1056-1066 1982

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

26. MOLECULAR MECHANISM OF ADAPTATION OF CELLS TO LOW LEVELS OF CARCINOGENIC AGENTS.
Villani G
Laboratoire de Pharmacologie et de Toxicologie Fondamentales, CNRS, 205, route de Narbonne, 31078 Toulouse Cedex, France
Pathol Biol (Paris); 30(2):117-123 1982
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27. MIGHT CANCER BE A FAILED RESPONSE TO RENEGADE MITOCHONDRIA?
Hartung J
Dept. Anesthesiology, State Univ. New York, Downstate Medical Center, Brooklyn, NY, 11203
J Theor Biol; 94(1):173-178 1982

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Anisimov VN
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Usp Sovrem Biol; 92(3):455-472 1981
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29. RELATION OF NEUROLEPTIC DRUGS TO DEVELOPMENT AND GROWTH OF MAMMARY TUMORS.
Meites J, Aylsworth CF
Dept. Physiology, Neuroendocrine Res. Lab., Michigan State Univ., East Lansing, MI, 48824
Banbury Rep; 8:365-376 1981

30. THE ACTIONS OF INSULIN AS A HORMONAL FACTOR IN BREAST CANCER.
Hilf R, Siiteri PK, Shellabarger, Korenman SG, Rosen, Nandi
Dept. Biochemistry and Univ. Rochester Cancer Center, Univ. Rochester, Rochester, NY, 14642
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31. ONCOGENES.
Bishop JM
Univ. California, San Francisco, CA
Sci Am; 246(3):80-84,87-92,154 1982

32. HUMAN CANCERS AND HUMAN VIRUSES.
Waterson AP
Royal Postgraduate Medical Sch., London W12 0HS, England
Br Med J; 284(6314):446-448 1982

33. THE IMMUNOLOGY OF CANCER OF THE HEAD AND NECK WITH PARTICULAR REFERENCE TO ORAL CANCER.
Scully C
Univ. Dept. Oral Medicine and Pathology, Immunology Unit, Glasgow Dental Hosp., 378 Sauchiehall St., Glasgow G2 3JZ, Scotland
Oral Surg; 53(2):157-169 1982

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Trosko JE, Chang CC, Warren ST, Liu PK, Wade MH, Tsushimoto G
Dept. Pediatrics and Human Development, Michigan State Univ., Coll. Human Medicine, East Lansing, MI, 48824
Gann Monogr Cancer Res; 27:159-179 1982

35. BIOLOGICAL MONITORING IN THE IDENTIFICATION OF THE CANCER RISK OF INDIVIDUALS EXPOSED TO CHEMICAL CARCINOGENS.
Vainio H, Sorsa M, Rantanen J, Hemminki K, Aitio A
Inst. Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland
Scand J Work Environ Health; 7(4):241-251 1981

36. A CRITICAL REVIEW OF BIOLOGICAL METHODS FOR THE DETECTION OF FUNGAL TOXINS IN FOODS AND FOODSTUFFS.
Watson DH, Lindsay DG
Food Science Div., Ministry of Agriculture, Fisheries, and Food, Great Westminster House, Horseferry Road, London SW1P 2AE, England
J Sci Food Agric; 33(1):59-67 1982

37. PITUITARY AND STEROID HORMONES IN RADIATION-INDUCED MAMMARY TUMORS.
Shellabarger CJ
Medical Dept., Brookhaven National Lab., Upton, NY, 11973
Banbury Rep; 8:339-351 1981

38. ASPERGILLUS NIDULANS: SYSTEMS AND RESULTS OF TESTS FOR CHEMICAL INDUCTION OF MITOTIC SEGREGATION AND MUTATION. I. DIPLOID AND DUPLICATION ASSAY SYSTEMS. A REPORT OF THE U. S. EPA GENE-TOX PROGRAM.
Kafer E, Scott BR, Dorn GL, Stafford R
Dept. Biology, McGill Univ., 1205 Ave. Docteur Penfield, Montreal H3A 1B1, Canada
Mutat Res; 98(1):1-48 1982

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39. MATHEMATICAL MODELS OF THE CELL CYCLE WITH A VIEW TO TUMOR STUDIES.
Bertuzzi A, Gandolfi A, Giovenco MA
Centro di Studio dei Sistemi di Controllo e Calcolo Automatici del C.N.R., Via Eudossiana 18, 00184 Rome, Italy
Math Biosci; 53(3/4):159-188 1981

40. NEOPLASMS IN DOMESTIC ANIMALS: A REVIEW OF EXPERIMENTAL AND SPONTANEOUS CARCINOGENESIS.

Madewell BR

Section Clinical Oncology, Dept. Veterinary Surgery, Univ. California, Davis, CA, 95616

Yale J Biol Med; 54(2):111-125 1981

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. CANCER IN LIBERIA: A REVIEW OF CASES REGISTERED FROM THE LIBERIA CANCER REGISTRY 1973-1977.

Sobo AO
JFK Medical Center, P.O. Box 1973, Monrovia, Liberia
Cancer; 49(9):1945-1951 1982

Data from the Liberia Cancer Registry are reviewed for a 5-yr period. Information collected included name, age, sex, tumor site, and histologic diagnosis. Collection of accurate data was complicated by factors including inadequate diagnostic facilities, lack of documentation of patient age, and the tendency for more affluent patients to seek treatment abroad. During the first 5 yr of the registry 1,652 patients (766 men and 866 women) were registered. The total incidence of cancers was 22.5 cases/100,000 population. The incidence was fairly constant during the period, except for a decline in the last yr. Approx 10% of patients were of undetermined age. Among males the most common cancers included cancer of the liver (16.2% of cases), cancer of the prostate (11.0%), Hodgkin's disease (8.5%), Burkitt's lymphoma (8.2%), and cancer of the bladder (7.7%). Among females the most common cancers included cancer of the cervix (28.1% of cases), cancer of the breast (11.1%), cancer of the ovary (10.4%), cancer of the liver (5.4%), choriocarcinoma (4.9%), and Burkitt's lymphoma (4.2%). The frequency of lung cancer was low in both sexes, and skin cancers were less frequent than those reported in Senegal and the Cameroons. (18 Refs)

2. MORTALITY OF SHIPHAM RESIDENTS: 40-YEAR FOLLOW-UP.

Inskip H, Beral V, McDowall M
Dept. Medical Statistics and Epidemiology, London Sch. Hygiene and Tropical Medical, Keppel St., London WCIE 7HT, England
Lancet; 1(8277):896-899 1982

The 1939 populations of Shipham, a village in Somerset with high soil-cadmium levels, and a nearby control village have been followed for 40 years. Death certificates were obtained for those who had died, and the mortality rates were compared with those for England and Wales. Small excesses of hypertensive, cerebrovascular, and genitourinary disease were noted in Shipham but not in the control village. These conditions have been associated with cadmium toxicity, and so it is possible that cadmium had some influence on the disease pattern in Shipham; but if so, the effect was slight. By contrast, fewer deaths than expected from respiratory disease and cancers were observed in both villages. This gave rise to all-cause mortality rates in Shipham and the control village which were similar and well below the national average. (Author abstract) (24 Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

3. MORTALITY AND CANCER MORBIDITY AMONG WORKERS IN THE RUBBER TIRE INDUSTRY.

Delzell E, Lewis J, Monson RR
(c/o Monson) Dept. Epidemiology, Harvard Sch. Public Health, 677 Huntington Ave., Boston, MA, 02115
Am J Industr Med; 2(3):209-216 1981

Mortality and cancer incidence were evaluated retrospectively in 1,792 white men employed at a rubber tire plant between 1954 and 1976. The 1,792 workers had accumulated 26,839 person-yr of follow up. Among men employed for 10 yr or more, overall cancer mortality was approx 19% higher than that expected in Connecticut white males, whereas cancer incidence for all sites combined was similar in the two groups. Excesses in deaths and incident cases for cancers of the buccal cavity and pharynx, large intestine, pancreas, and kidney were observed. The workers also showed excesses in deaths from cancers of the digestive organs and peritoneum and incident cases of cancer of the bronchus and lung. No increase in occurrence of stomach or bladder cancer or of leukemia was seen. Limitations of the data are discussed in terms of interpreting the results. As the workers investigated were young (93% total person-yr less than 65 yr old), and because estimates of cancer excesses were conservative in this study, cancer mortality and morbidity should continue to be monitored in the rubber industry. (15 Refs)

4. EPIDEMIOLOGICAL FEATURES OF WILMS' TUMOR: RESULTS OF THE NATIONAL WILMS' TUMOR STUDY.

Breslow NE, Beckwith JB
Dept. Biostatistics SC-32, Univ. Washington, Seattle, WA, 98195
JNCI; 68(3):429-436 1982

Nearly 2,000 children with Wilms' tumor registered in a national clinical trial during 1969-81 showed high rates of aniridia, hemihypertrophy, cryptorchidism, hypospadias, and other genitourinary anomalies. Patients with bilateral disease, who constituted 5% of the total, had younger ages at diagnosis and an increased incidence of congenital anomalies and renal blastemal rests. Those with multicentric unilateral lesions had more blastemal rests but were otherwise indistinguishable from the unicentric cases. The 20 familial cases had none of the features usually associated with genetic tumors: neither younger ages nor an increase in bilaterality nor associated congenital anomalies. These observations suggest that the fraction of Wilms' tumors that is due to an inherited mutation may be substantially smaller than previously supposed and support the concept that the disease arises from a variety of pathogenetic pathways. (Author abstract) (38 Refs)

5. THE CARCINOGENIC EFFECT OF AROMATIC AMINES: AN EPIDEMIOLOGICAL STUDY ON THE ROLE OF O-TOLUIDINE AND 4,4'-METHYLENE BIS(2-METHYLANILINE) IN INDUCING BLADDER CANCER IN MAN.

Rubino GF, Scansetti G, Piolatto G, Pira E
Inst. Occupational Health, Turin Univ., CTO- Via Zuretti, 29-10126 Torino, Italy
Environ Res; 27(2):241-254 1982

Cause-specific mortality of 906 workers first employed 1922-1970 in a dyestuff factory in Northern Italy was compared to

national figures; a marked excess of bladder cancer was observed (36 observed vs 1.23 expected deaths). The mean latent period was 25 years. The excess was higher among those with longer duration of exposure. Some excess of mortality from lung cancer, laryngeal cancer, and esophageal cancer was also found, but a clear explanation could not be provided regarding the causal role of aromatic amines. Mortality from bladder cancer was very much higher among those exposed in benzidine and naphthylamines manufacture as compared to those only exposed in use or intermittent contact. Excess bladder cancer was also very high among workers in fuchsin manufacture. There is evidence that O-toluidine and 4,4'-methylene bis(2-methylaniline) should be implicated in such excess mortality. Caution in handling these compounds is therefore suggested and the need for further studies to confirm such findings is stressed. (Author abstract) (19 Refs)

6. OCCUPATIONAL BLADDER CANCER AND CIGARETTE SMOKING IN WEST YORKSHIRE.

Cartwright R
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Scand J Work Environ Health; 8(Suppl1):79-82 1982

Results of the preliminary analysis of the first 1,000 cases of bladder cancer pooled from three hospital districts, Huddersfield with both high mortality and morbidity, Bradford with high morbidity and low mortality, and Wakefield with both low morbidity and mortality, are presented. All cases prevalent at the onset of the study in 1978 together with all incident cases occurring since, up to 1980 were included. All prevalent cases were matched with one hospital referent and all incident cases with two. The following information was collected: identification, coffee and alcohol drinking habits, smoking habits, saccharin use, past medical history, past drug treatment, occupational history, hobbies, and family history. Results of the analysis for cigarette smoking showed a statistically significant risk for bladder cancer. The risks associated with the cases that had worked for at least 6 mo in seven risk occupations are summarized. The chemical industry workers included a preponderance of process workers in the dye manufacturing industry. Summary of the risk ratios for contemporaneous smokers and nonsmokers in three occupations is presented. The differences between the pair of risk ratios were statistically significant for dye manufacturers but not for dye users or printers. The age of workers at the beginning of work in the dye manufacturing industry influenced the subsequent risk of developing bladder cancer. The actual length of employment and the date of beginning the work were both important variables. (11 Refs)

7. CALCULATION OF POTENTIAL BIAS IN THE ODDS RATIO ILLUSTRATED BY A STUDY OF SACCHARIN USE AND BLADDER CANCER.

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Environ Res; 27(2):298-306 1982

Criticisms of questionnaire studies often emphasize methodological weaknesses which, if unexamined, may lead to biased risk estimates. Observational studies of the relationship between saccharin use and the risk of bladder cancer illustrate this point. This paper describes the potential biases due to misclassification and to the use of prevalent rather than incident cases in a recent report by I.I. Kessler and J.P. Clark (1978, J Amer Med Assoc 240, 349-355). Assuming the true risk ratio is greater than unity, nondifferential misclassification of exposure leads to an observed odds ratio or relative risk closer to the null value. Differential misclassification of exposure results in either an overestimate or an underestimate of the true risk. Varying the sensitivity and specificity of the exposure among cases and controls alters the risks ratios dramatically. The use of prevalent rather than incident cases in a hospital-based-control study does not affect the risk measure unless it can be demonstrated that exposure differentially influences the force of morbidity or mortality. The exclusion of a large number of deceased cases in Kessler and Clark's report may underestimate the risk ratio by 18-28%. Unless other factors are discovered, the identified biases will not meaningfully alter the conclusion that there is no association between saccharin use and bladder cancer in Kessler and Clark's study. (Author abstract) (15 Refs)

8. CONCENTRATION 239,240 PU IN HUMAN AUTOPSY TISSUES. PRELIMINARY REPORT OF A COMPARATIVE STUDY ON DIFFERENT POPULATIONS.

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Div. Radioecology, Natl. Inst. Radiological Sciences, 3609 Isozaki, Nakaminato-shi, 311-12, Japan
J Radiat Res (Tokyo); 22(4):373-380 1981

Concentrations of 239,240Pu were studied in autopsy material of males and females (21-69 yr old) who died in Tokyo in 1970. Lung and liver specimens were obtained from 10 subjects; kidney samples were also obtained from five. Bone samples were obtained from another 10 subjects, including some of the above. Tissue ash samples were analyzed for 239,240 Pu content by a radiochemical procedure and the alpha spectrometric method developed at the Los Alamos National Laboratory. Data obtained from the Japanese subjects' tissues were compared with similar data from the Los Alamos data base for 1970 autopsy cases from the United States. Lung, liver, and kidney 239,240 Pu concentrations in the Japanese population were significantly lower than in the United States populations, whereas concentration of 239,240 Pu in vertebra was significantly higher in Japan. Bovine liver and kidney samples from Japan showed no measurable concentration of 239,240 Pu. The discrepancies in values between the United States and Japan indicate the need for further studies of concentration of Pu and other transuranic elements in human tissues. (16 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

9. CARCINOGENICITY OF PHENACETIN: LONG-TERM FEEDING STUDY IN B6C3F1 MICE.

Nakanishi K, Kurata Y, Oshima M, Fukushima S, Ito N
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Int J Cancer; 29(4):439-444 1982

Groups of 52 B6C3F1 mice of each sex were maintained on a diet containing 1.25 of 0.6% phenacetin for 96 wk and then fed a basal diet for 8 wk. Control groups consisted of 50 mice of each sex and were fed a basal diet for 104 wk. All animals were killed at the end of the experiment and all organs were examined histopathologically. Mice that died during the experiment were also autopsied and those that survived for more than 57 wk, when the first tumor was observed, were also in-

cluded in the effective number of mice. Tumors were found in the kidney, liver, lung, skin, hematopoietic system (leukemia or lymphoma) and occasionally in some other organs. The dose-related induction of renal cell tumors in the male mice fed phenacetin was clearly demonstrated in this experiment. Urinary bladder lesions that developed in the mice of either sex fed 1.25% phenacetin were also considered to be due to the tumorigenicity of phenacetin. Tumors of other organs in either the phenacetin-treated or the control group were regarded as strain-related spontaneous tumors of B6C3F1 mice. (Author abstract) (20 Refs)

10. CARCINOGENICITY AND TOXICITY OF 1,2-DIBROMOETHANE IN THE RAT.

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Toxicol Appl Pharmacol; 63(2):155-165 1982

The chronic effects of 1,2-dibromoethane (ethylene dibromide, EDB) were investigated in rats. Three experimental groups were studied: (1) inhalation of 20 ppm EDB over an 18-mo period, (2) 0.05% disulfiram (DS) in the diet for 18 mo, and (3) combined treatment of 20 ppm EDB + 0.05% DS. Rats receiving DS only showed less body wt gain than controls or EDB-exposed rats over the 18-mo period. Rats receiving EDB + DS had lower wt gain than animals receiving either EDB or DS alone. A correlation between low food consumption and low body wt gain was found in rats treated with DS or DS + EDB. EDB-treated or EDB + DS-treated rats exhibited high mortality compared with control rats or those treated with DS alone. While hematological findings were normal for EDB-treated rats, EDB + DB treatment resulted in low hematocrit, hemoglobin, and red blood cell counts. Male rats treated with DS alone did not exhibit any significant histopathological changes except for a higher incidence of hemosiderosis of the spleen; females had a higher incidence of mammary tumors and of hemosiderosis of the spleen. Rats inhaling EDB alone had a higher incidence of tumors, in one or both sexes, in the spleen, adrenal, subcutaneous mesenchymal tissue, and mammary gland compared to controls. Combined treatment with EDB + DS caused an increased incidence of tumors in one or both sexes, in the liver, kidneys, thyroid, lungs, and spleen compared to treatment with either EDB or DS alone. Combined treatment also caused a higher incidence of atrophy of the testes and spleen compared to treatment with EDB alone. These results indicate that DS, a drug used in the treatment of chronic alcoholism, enhances the toxicity and carcinogenicity of EDB. Such an effect may be significant in evaluating the hazards of industrial exposure to EDB in workers who are being treated in alcohol control programs. (37 Refs)

11. CARCINOGENICITY OF 2-AMINO-4-(5-NITRO-2-FURYL)THIAZOLE IN RATS BY ORAL AND SUBCUTANEOUS ADMINISTRATION.

Wang CY, Kamiryo Y, Croft WA
Dept. Chemical Carcinogenesis, Michigan Cancer Foundation, 110 E. Watten Ave., Detroit, MI, 48201
Carcinogenesis; 3(3):275-277 1982

Female Fischer rats were divided into two groups and fed either basal diet or basal diet containing 0.166% 2-amino-4-(5-nitro-2-furyl)thiazole for 52 wk followed by basal diet for an additional 16 wk. Out of the 24 rats fed 2-amino-4-(5-nitro-2-furyl)thiazole, 23 had forestomach tumors, 4 had fibroadenomas and 2 had adenocarcinomas in the mammary glands, 2 had renal pelvic carcinomas, 5 had papillomas and 6 had carcinomas in the bladder, and 2 had cutaneous tumors. None of the 10 rats fed basal diet developed tumors. In another study, 2-wk-old Fischer rats of both sexes were injected sc once a wk for the first 8 wk with 2-amino-4-(5-nitro-2-furyl)thiazole at a dose of 10 mg/kg and then 1.4 mg/rat for an additional 46 wk. The control rats were injected with solvent (dimethyl sulfoxide:water, 1:1) only. The experiment was terminated at the end of 58 wk. Malignant fibrous histiocytomas were found in 5 out of 8 male rats and 4 out of 11 female rats, and and angiosarcoma was found in one out of eight male rats injected with 2-amino-4-(5-nitro-2-furyl)thiazole. None of the control rats developed tumors. (Author abstract) (12 Refs)

12. CARCINOGENICITY EXAMINATION OF INFLORESCENCE OF ZINGIBER MIOGA ROSCOE.

Hirono I, Mori H, Kato K, Hosaka S, Aiso S
Dept. Carcinogenesis and Cancer Susceptibility, Inst. Medical Sciences, Univ. Tokyo, Minato-ku, Tokyo 108, Japan
Cancer Lett; 15(3):203-208 1982

Inflorescence of Zingiber mioga, a vegetable commonly used in Japan, was tested for carcinogenicity on oral administration in ACI rats (10 males, 10 females, 1-1.5 mo old) fed a mioga diet for 365 days and Fischer 344 rats (15 males, 15 females, 1.5 mo old) fed a mioga diet for 639 days. Eighteen of 20 ACI rats survived more than 336 days and 14 survived until the end of the experiment on day 480. The tumors found in rats are tabulated. One male and one female rat had urinary papilloma, and females had transitional cell carcinoma (TCC) of the urinary bladder (UB). In the control group one male developed interstitial cell tumor of the testis (ICTT) and one female TCC of the UB. A significant difference was observed between the incidence of UB tumors in female rats in the experimental and control groups. All Fischer 344 rats on the mioga diet survived for more than 391 days and 22/30 rats survived until the end of the experiment. No UB tumors were observed in the experimental or control group. ICTT and pituitary and lung adenomas were found in both the experimental and control group. No significant difference was observed in the incidence of these tumors. Three sc fibromas, one squamous cell carcinoma of the salivary glands, and three adrenal cortical adenomas were found in the control group. The incidences of these tumors were also not significantly different in the experimental and control groups. (9 Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

13. ORGAN-SPECIFIC PROMOTING EFFECTS OF PHENOBARBITAL SODIUM AND SODIUM SACCHARIN IN THE INDUCTION OF LIVER AND URINARY BLADDER TUMORS IN MALE F344 RATS.

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JNCI; 68(3):497-500 1982

Studies were conducted to determine whether initial treatment with N-2-fluorenylacetamide (2-FAA) or N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN) followed by treatment with either phenobarbital sodium (PB) or sodium saccharin (SS) induced or enhanced liver and/or bladder tumorigenesis. Male inbred F344 rats were given 0.05% PB and 5.0% SS in the diet

for 32 wk after 4-wk administration of 0.02% 2-FAA or 0.01% BBN. PB significantly enhanced hepatocarcinogenesis after 2-FAA treatment and induced hyperplastic liver nodules after BBN treatment. The SS significantly enhanced induction of bladder hyperplasias, but not papilloma after BBN treatment, and induced bladder hyperplasias after 2-FAA treatment. However, PB had no effect on the bladder and SS had no effect on the liver after either 2-FAA or BBN treatment. The data indicate that although 2-FAA and BBN have tumor-initiating effects in the liver and urinary bladder, the tumor-promoting effects of PB and SS are organ-specific. The tumor-promoting effect of PB for the liver is relatively greater than that of SS for the urinary bladder. (Author abstract) (25 Refs)

14. EFFECT OF ASCORBIC ACID ON THE CARCINOGENIC ACTIVITY OF P-HYDROXYPHENYLLACTIC ACID.

Khar'kovskaia NA, Khrustalev SA, Zharova EI, Raushenbakh MO
Dept. Experimental Animals, All-Union Cancer Res. Center, Moscow, USSR
Biull Eksp Biol Med; 92(1):64-66 1982

Anticarcinogenic effect of ascorbic acid (AA) during carcinogenesis induced by tyrosine metabolites was studied in C57BL mice. The animals were divided into two groups: mice in Group 1 received para-hydroxyphenyllactic acid alone (PHPLA: 5 mg, sc 2x/wk, 5 wk), and mice in Group 2 received the PHPLA in combination with AA (250 mg/100 ml in drinking water). The animals were followed up for 20-22 mo. Tumors were observed in 55% of the mice in Group 1 and in 22.5% of those in Group 2. Most tumors in both groups had histologies of mixed lymphosarcoma. In addition to the lymphosarcoma, mice in Group 1 developed bladder precancer and hyperplasia, while mice in Group 2 were free of bladder precancer and had an incidence of hyperplasia of bladder epithelium which was 3x lower than that in Group 1. The AA administration increased the latent period of tumor development. (8 Refs) (In RUS)

15. INHIBITION OF CHEMICAL CARCINOGENESIS BY RETINOIDS.

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J Am Acad Dermatol; 6(4,part2):809-814 1982

Experiments involving two-stage skin carcinogenesis in mice, the induction of bladder tumors in rats or mice by N-methyl-N-nitrosourea (MNU) or N-butyl-N-(4-hydroxybutyl)nitrosamine (OH-BBN), the induction of mammary tumors in rats by MNU, and the induction of esophageal tumors in rats by N-methyl-N-benzylnitrosamine have demonstrated several important structure-activity relationships in the inhibition of chemical carcinogenesis by retinoids. The aromatic ring, side chain, and polar terminal groups of the retinoid molecule have important effects on the agent's organ distribution and thus its anticarcinogenic activity. Retinoids that significantly inhibit OH-BBN bladder carcinogenesis include 13-cis-retinoic acid (c-RA), ethyl retinamide, 13-cis-ethyl retinamide, 2-hydroxyethyl retinamide, 4-hydroxyphenyl retinamide (4-HPR), 13-cis-4-hydroxyphenyl retinamide, and 2-hydroxypropyl retinamide. Retinoic acid (RA) is a less favorable preventer of MNU-induced mammary tumors in rats than 4-HPR, because 4-HPR accumulates to a lesser extent in the liver and so is less hepatotoxic than RA. Synergistic interactions between retinoids (eg, RA or 4-HPR) and hormonal treatments in MNU mammary carcinogenesis have been discovered. Retinoid treatment from the time of carcinogen administration or the first excision of a carcinogen-induced tumor has greater chemopreventive activity than delayed treatment. The efficacy of delayed retinoid treatment largely depends on the tumor's latent period. The authors' current research involves the identification of new retinoids having lower toxicity and higher chemopreventive activity, combination treatments having synergistic antitumor activity, and the mechanisms of action of the retinoids. (28 Refs)

16. RETINOID-BINDING PROTEINS.

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J Am Acad Dermatol; 6(4,part2):583-590 1982

Plasma retinol binding protein (PRBP), cellular retinol binding protein (CRBP), and cellular retinoic acid binding protein (CRABP) are immunologically distinct from each other. PRBP, produced in the liver and catabolized mainly in the kidneys, is responsible for the delivery of retinol to its extrahepatic sites of action. No disease has yet been identified in which PRBP was totally absent or immunologically abnormal. The results of preliminary experiments suggest that CRBP may be identical in different tissues and different species. Comparable information is not yet available for CRABP. The tissue levels and distributions of CRBP and CRABP in animal and human tissues are distinct from each other. Little is known about the factors influencing and regulating the tissue levels and metabolism of CRBP and CRABP. Retinoid-binding proteins (notably CRABP) have been identified in many tumors and cell lines. It has been reported that the binding ability of synthetic retinoids for the intracellular binding proteins (notably CRABP) tends to correlate with the ability of the retinoid to influence epithelial cell differentiation and/or tumor growth in vivo or in vitro. Further research is needed to define the biochemical processes mediated by these substances. (57 Refs)

17. THE ROLE OF URINE IN A PATIENT WITH A BLADDER NEOPLASM.

Melicow MM
Dept. Uropathology Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY
J Urol; 127(4):660-664 1982

A review was done on reported cases of spontaneous regression of superficial bladder tumors in which cystectomy was preceded by bilateral ureterosigmoidostomy (the interval ranging from 21 days to 6 mo). In every case in which the tumors were superficial complete disappearance of the papillary masses was observed by the naked eye and by microscopic examination. Tumor cells persisted in those cases in which the bladder wall was involved. I propose that the urine of the patient acts as a promoter to hyperplasia and neoplasia on foci of defective urothelial cells whose special coding apparatuses had been injured or destroyed by a carcinogen. The latter need no longer be present nor need there be exposure to co-carcinogen(s), such as is associated with excess alcohol intake or cigarette smoke inhalation. Tumor cells that were found in the excised bladder wall were cells that had become invasive (cancerous) and were no longer dependent (Author abstract) (22 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

18. INHIBITION OF DNA SYNTHESIS AND ALTERATION TO DNA STRUCTURE BY THE PHENACETIN ANALOG P-AMINOPHENOL.

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Biochem Pharmacol; 31(7):1425-1429 1982

p-Aminophenol a structural analog and minor metabolite of phenacetin has previously been shown to be a potent nephrotoxic agent. In this report we have shown that p-aminophenol has a marked effect on DNA function and structure. DNA synthesis was inhibited in a dose-dependent manner in human lymphoblastoid cells after exposure to p-aminophenol. Results suggest that DNA synthesis is inhibited by the action of p-aminophenol on DNA structure. At low concentrations of p-aminophenol a reduction in the degree of supercoiling of cellular DNA is observed, as determined by sedimentation under neutral conditions. However at higher concentrations an increase in sedimentation of nucleoids (supercoiled molecules) is obtained which is indicative of an increased level of supercoiling or a more compact structural form of DNA due to folding or aggregation. The number of single strand breaks in DNA, when determined by sedimentation in alkaline sucrose gradients, increases with increasing dose of p-aminophenol. The increase in strand breakage observed at lower concentrations of p-aminophenol agrees with the reduced sedimentation rate obtained under neutral conditions. At higher concentrations of p-aminophenol the extent of breakage of DNA increases under alkaline conditions but an increase in sedimentation occurs under neutral conditions. (Author abstract) (23 Refs)

19. METABOLISM AND DNA BINDING OF BENZO[A]PYRENE IN CULTURED HUMAN BLADDER AND BRONCHUS.

Stoner GD, Daniel FB, Schenck KM, Schut HA, Goldblatt PJ, Sandwisch DW
Dept. Pathology, Medical Coll. Ohio, 3000 Arlington Ave., Toledo, OH, 43614
Carcinogenesis; 3(2):195-201 1982

The metabolism of benzo[a]pyrene (BP) was examined in explant cultures of human bladder and bronchus. Three-day cultures were exposed to radiolabeled BP for 24 hr, and the metabolism was determined by analysis of the level of binding of reactive metabolites to DNA, and by the release of metabolites into the medium. For a given individual, the DNA binding level and extent of metabolism was usually higher in the bladder than in the bronchus. In specimens obtained from 16 individuals, the average DNA-binding levels for BP-DNA adducts following a 24 hr exposure to 1 uM BP were 6.4 +-5.0 umol BP/mol deoxyribonucleotide for the bladder and 3.1 +-1.9 umol BP/mol deoxyribonucleotide for the bronchus. The major BP - DNA adduct in both tissues co-chromatographed with one of the adducts formed by reaction of r-7,t-8-dihydroxy-t-9,10-oxy-7,8,9,10 tetrahydrobenzo[a]pyrene with deoxyguanosine using high-pressure liquid chromatography. In tissues obtained from the same individual, the binding levels of BP metabolites to bladder cell DNA was not strongly correlated to that of bronchial cell DNA ($r = 0.54$). The medium of both tissues contained small amounts of free, unconjugated metabolites of BP (less than 3% of the total) and large amounts (30-85% of the total) of unidentified, highly polar material. Human bladder appears to be the most active human explant tissue yet studied with respect to its ability to activate BP to DNA binding forms. The relevance of this observation to human bladder cancer is, as yet, unknown. (Author abstract) (40 Refs)

20. METABOLISM OF BENZO(A)PYRENE IN RAT BY ORAL ADMINISTRATION.

Yamazaki H, Kumahashi H, Masuda N, Kishi T, Kakiuchi Y, Watabe K, Kondo M
(c/o Kakiuchi) Faculty Pharmaceutical Sciences, Kobe Gakuin Univ., 518, Arise, Igawadani, Tarumi, Kobe, 673, Japan
Chemosphere; 11(3):337-347 1982

Adult male Sprague-Dawley rats were given a single oral dose of tritiated (50 uCi) benzo(a)pyrene (BaP). They were sacrificed at hr 3, 7, 24, and 48. Organs, blood, and urine were assayed for BaP and metabolites. the urinary radioactivity was maximum at hr 7, decreasing slowly thereafter. Blood, kidney, liver, and lung radioactivity levels were all highest at hr 3, dropping sharply by hr 24. At hr 3 the liver contained a relatively high level of benzo(a)pyrene-9,10-diol, with lesser amounts of 3-hydroxybenzo(a)pyrene, benzo(a)pyrene-4,5-diol, benzo(a)pyrene-7,8-diol, benzo(a)pyrene-3,6-quinone, benzo(a)pyrene-1,6-quinone, and BaP. At hr 3 the kidney was highest in both quinones, with large amounts of all diols too. Peak amounts occurred in the lung at hr 7, mainly the two quinones and BaP; compared to all other sources the lung contained more metabolites and BaP at hr 48. At hr 3 in the blood the 9,10-diol and BaP were predominant; at hr 7, the 3-hydroxy metabolite prevailed. In contrast to the above sources, the urinary metabolites existed mainly as the glucuronides, mostly as the 3,6-quinone and 9,10-diol at hr 7. (19 Refs)

21. METABOLISM OF 3-HYDROXYBENZO(A)PYRENE IN RAT, ISOLATED HEPATOCYTES AND KIDNEY.

Yamazaki H, Kagita T, Fujiwara M, Kishi T, Kakiuchi Y, Watabe K, Kondo M
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Chemosphere; 11(3):349-353 1982

Adult male Sprague-Dawley rats were given an iv dose of tritiated (0.1 uCi) 3-hydroxybenzo(a)pyrene (3-OHBaP). Urine was collected at hr 24 and 48. The same amount of tritiated 3-OHBaP was also incubated with perfused rat hepatocytes and with sliced rat kidney at 37 C for 2 or 3 hr; extracts were obtained at hr 0.5, 1, 2, and 3 (kidney only). At hr 24 the urine contained benzo(a)pyrene-9,10-diol, benzo(a)pyrene-4,5-diol, benzo(a)pyrene-1,6-quinone, and 3-OHBaP. At hr 48 the urine still contained all of them, but the 9,10-diol was now present only as a glucuronide compared to none at hr 24. All of these metabolites and 3-OHBaP were found in the hepatocytes at all times except for no 1,6-quinone at hr 1, mainly as quinones at all times and 9,10-diol at hr 2. The 3-OHBaP was assayed only as a glucuronide; the 9,10-diol was never found as a glucuronide. In the kidney extracts only quinone metabolites were identifiable at hr 0.5 and 1. At hr 2 all the diols were present too, mainly 4,5-and 7,8-. At hr 3 not much change had occurred, but the 9,10-diol was present also as a glucuronide; 3-OHBaP was present as a glucuronide. (9 Refs)

22. METABOLISM OF PHENANTHRENE IN VARIOUS MARINE ANIMALS.

Solbakken JE, Palmork KH
Inst. Marine Res., Directorate of Fisheries, Nordnesparken 2, N-5011 Bergen, Norway
Comp Biochem Physiol [C]; 70(1):21-26 1981

Metabolites of phenanthrene (PA) were analyzed by combined gas chromatography-mass spectroscopy in tissues of flounder (Platichthys flesus), rainbow trout (Salmo gairdneri), spiny dogfish (Squalus acanthias), and Norway lobster (Nephrops norvegicus), which had been force fed PA at a rate of 21-337 mg/kg. Fish and crustaceans are able to metabolize PA to water-soluble conjugated and non-conjugated metabolites, which vary by species and in tissue distribution. (24 Refs)

23. DISTRIBUTION AND RETENTION OF BENZO(A)PYRENE IN RATS AFTER INHALATION.

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Inhalation Toxicology Res. Inst., Lovelace Biomedical and Environmental Res. Inst., P.O. Box 5890, Albuquerque, NM, 87185
Toxicol Lett; 11(1/2):35-42 1982

The distribution and retention of inhaled radioactive benzo(a)pyrene (BA) was determined in rats. Twenty-four male Fischer-344 rats were exposed for 1 hr to BAP (500 ug/liter air). Tissue, urine, and fecal radioactivity analyses were performed 0, 3, 6, 12, 24, or 48 hr after exposure. Significant amounts of BAP were found in the stomach, small intestine, trachea, lungs, nasal turbinates, larynx, tracheobronchial lymph nodes, kidneys, and liver immediately after exposure. Fifty per cent of the radioactivity cleared from the respiratory tract within 2-3 hr; the remaining cleared between 25 and 56 hr. Fifty per cent clearance of BAP from the liver was obtained in 6 hr. BAP and metabolite concentration in the kidney reached a max value 6 hr after exposure; subsequent clearance was at a constant rate. Radioactivity levels in the spleen, brain, and testes were lower than other major organs, and remained constant for 24 hr after exposure. Radioactivity accumulated rapidly in the cecum and large intestines and subsequently decreased at a constant rate. Excretion of radioactivity was primarily via the feces. Additional studies are necessary to determine the potential mutagenic or carcinogenic risk of BAP exposure in some tissues. (16 Refs)

24. METABOLISM, DISTRIBUTION, AND EXCRETION OF THE FLAME RETARDANT, TRIS(2,3-DIBROMOPROPYL) PHOSPHATE (TRIS-BP) IN THE RAT: IDENTIFICATION OF MUTAGENIC AND NEPHROTOXIC METABOLITES.

Lynn RK, Garvie-Gould C, Wong K, Kennish JM
Dept. Pharmacology, Oregon Health Sciences Univ., Portland, OR, 97201
Toxicol Appl Pharmacol; 63(1):105-119 1982

Metabolism and distribution of tris(2,3-dibromopropyl) phosphate (Tris-BP) were followed in male Sprague-Dawley rats for 5 days after iv injection of 14C-Tris-BP. Approx 58% of radiolabel was excreted within 24 hr, and 86% by 5 days. At this time approx 9% of the dose remained in the body (95% recovery). Studies in several animals with exteriorized bile ducts showed that approx 34% of the dose was excreted in the bile at 24 hr, but that a minimum of 74% of this was reabsorbed. High pressure liquid chromatography demonstrated numerous radiolabeled components, of which bis(2,3-dibromopropyl) phosphate (Bis-BP) and 2,3-dibromopropanol (DBP) were identified. Tris-BP disappeared rapidly in tissues and was undetectable at 8 hr, but the half-life of Bis-BP was relatively long. Bis-BP concentrated in lung, muscle, fat, and especially blood, where it accounted for approx 90% of the radiolabel at 30 min and 8 hr. At 5 days the concentration of radiolabel was highest in the kidneys, 11x the av whole body concentration. This may be related to the polyuria induced by large doses of Tris-BP. In Ames mutagenicity testing on TA100 and TA1535, with microsomal activation, Tris-BP was most mutagenic, with Bis-BP and DBP approx equal at all concentrations except the highest (1,000 nanomole/plate), where Bis-BP was approx 80% more active. Previous work on Tris-BP is discussed and compared with these findings. (21 Refs)

25. INTRACELLULAR INTERACTION AND METABOLIC FATE OF ARSENITE IN THE RABBIT.

Marafante E, Rade J, Sabbioni E, Bertolero F, Foa V
Chemistry Div., Commission European Communities, JRC-Ispra Establishment, I-21020 Ispra (Va), Italy
Clin Toxicol; 18(11):1335-1341 1981

The association of arsenic with subcellular components was studied in male albino rabbits, in order to evaluate the role of these interactions in the metabolism of sodium arsenite. Distribution in the organs at different times after injection of 100 ug As/rabbit and intracellular distribution at different times after injection of the same concentration of As in nanog/g tissue are reported. Arsenic was found at subcellular levels mainly in the nuclear and soluble fractions of liver, kidney, and lung tissues. (9 Refs)

26. CYTOSOLIC AND NUCLEAR BINDING OF 2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN TO THE AH RECEPTOR IN EXTRA-HEPATIC TISSUES OF RATS AND MICE.

Mason ME, Okey AB
(c/o Okey) Div. Clinical Pharmacology, Dept. Pediatrics, Hosp. Sick Children, 555 University Ave., Toronto, Ontario M5G 1X8, Canada
Eur J Biochem; 123(1):209-215 1982

Induction of aryl hydrocarbon hydroxylase (cytochrome P1-450) is mediated by the Ah receptor which initially binds inducing chemicals in the cytoplasm, after which the inducer-receptor complex translocates into the nucleus. Ah receptor can be detected and quantified by sucrose-density-gradient analysis of its binding to 2,3,7,8-tetrachloro[3H]dibenzo-p-dioxin. Labeling in vitro of cytosols from C57BL/6J mice and Sprague-Dawley rats reveals Ah receptor in several tissues, with concentrations in the rank order for C57BL/6J mice: liver greater than lung much greater than kidney approx = thymus approx = small intestine greater than prostate; for Sprague-Dawley rats: liver approx = lung approx = thymus much greater than small intestine much greater than greater than kidney. Cytosol receptor was not detectable by assays in vitro on skin, skeletal muscle, heart, brain or testis of C57BL/6J mice or Sprague-Dawley rats, nor was specific receptor detectable in cytosol from any tissue of genetically 'non-responsive' DBA/2J mice. Injection in vivo of 2,3,7,8-tetrachloro[3H]dibenzo-p-dioxin led to recovery of specific nuclear Ah receptor from liver, lung and kidney of both genetically 'responsive' C57BL/6J mice and 'non-responsive' DBA/2J mice as well as Sprague-Dawley rats. Nuclear Ah receptor concentrations were lower in DBA/2J mice than in C57BL/6J mice receiving the same dose, and nuclear receptor was detectable only with injection of high doses of 2,3,7,8-tetrachloro[3H]dibenzo-p-dioxin. Although cytosolic Ah receptor in DBA/2J mice appears to be 'defective' and cannot be detected directly by assays in vitro, recovery of

specific receptor from nuclei of DBA/2J tissues implies that binding of 2,3,7,8-tetrachloro[3H]dibenzo-p-dioxin to Ah receptor does occur in vivo in these animals; this may explain the ability of 'non-responsive' DBA/2J mice to exhibit induction of aryl hydrocarbon hydroxylase when treated with the very potent inducer, 2,3,7,8-tetrachlorodibenzo-p-dioxin. (Author abstract) (12 Refs)

27. DNA DAMAGE IN LIVER, KIDNEY, BONE MARROW, AND SPLEEN OF RATS AND MICE TREATED WITH COMMERCIAL AND PURIFIED ANILINE AS DETERMINED BY ALKALINE ELUTION ASSAY AND SISTER CHROMATID EXCHANGE INDUCTION.

Parodi S, Pala M, Russo P, Zunino A, Balbi C, Albini A, Valerio F, Cimberle MR, Santi L

Dept. Oncology, Istituto Scientifico per lo Studio e la Cura dei Tumori, 16132 Genoa, Italy

Cancer Res; 42(6):2277-2283 1982

Aniline of unknown purity has been reported to induce spleen hemangiosarcoma in rats. Aniline has been found to be negative in terms of mutagenicity in both bacteria and yeasts. We have found that both commercial (already rather pure) and repurified aniline are clearly positive to a similar extent in inducing DNA damage in vivo in liver and kidney of rats. Both the commercial and repurified product are also clearly positive in induction of sister chromatid exchanges in vivo in male Swiss mice bone marrow cells. Liver, kidney, and bone marrow DNA damage was absent in male Swiss mice. (Author abstract) (30 Refs)

28. DISTURBANCES IN LYSOSOMAL ENZYME ACTIVITIES IN RATS FOLLOWING EXPERIMENTAL POSTRADIATION DISEASE.

Drozdz M, Piwowarczyk B, Olczyk K, Pikula-Zachara M

Zakład Chemii Klinicznej, Instytut Farmakodynamiki i Analytiki Medycznej Sl. Am, ul. Borowkowa 24, 40-692 Katowice, Poland

Med Pr; 32(3):201-206 1981

The effect of irradiation (500 rads) on lysosomal enzyme activities in serum, leukocytes, liver, kidneys, lungs, and heart of 6-mo-old male Wistar rats was studied 30 days after irradiation. The increased acid phosphatase (AP), beta-glucuronidase and beta-acetylglucosaminidase activities in the tissues were indicative of the labilizing effect of irradiation on lysosomal membranes. Kidneys, lungs and liver were found to be the most radiosensitive organs. The AP activity showed the greatest increase in serum and leukocytes. The activities of all enzymes examined were reduced in hepatic lysosomes. (55 Refs) (In POL)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

29. CORRELATIONS BETWEEN CELL SURFACE PROTEASE ACTIVITIES AND ABNORMALITIES OF OCCLUDENS JUNCTIONS IN RAT BLADDER CARCINOMA IN VITRO.

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Dept. Pathology, Rush-Presbyterian-St. Luke's Medical Center, 1753 West Congress Parkway, Chicago, IL, 60612

Cancer Res; 42(6):2289-2297 1982

Microenvironmental alterations, ie, proteolytic enzymes, may play a causative role in abnormalities of zonulae occludentes. To test this hypothesis, we compared in vitro the ultrastructure of three carcinoma cell lines which were derived from N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide-induced tumors of the rat urinary bladder. One of these lines had a high cell surface protease activity; the other two lines exhibited relatively low activities. Quantitative electron microscopy data revealed differences in configuration and distribution of zonula occludens-intramembrane fibrils among these cell lines, as indicated by means and standard deviations of zonulae occludens widths, and numbers of intramembrane fibrils. Although the total length of the intramembranous fibrils per square micrometer of occludens junction area was not statistically different in the three lines, junctional morphology varied greatly. Thus, carcinoma cells with high surface protease activities are able to synthesize near-normal amounts of intramembrane fibrils but are unable to assemble normal zonulae occludentes. This indicates that alterations in zonula occludens morphology, which have been induced by exogenous proteolytic enzymes, are identical to those observed in a cell line with high cell surface protease activity. (Author abstract) (42 Refs)

30. A HISTOCHEMICAL AND ULTRASTRUCTURAL STUDY OF HUMAN URETHRAL UROEPITHELIUM.

Alm P, Colleen S

Dept. Pathology and Urology, Univ. Hosp. Lund, Lund, Sweden

Acta Pathol Microbiol Scand [A]; 90(2):103-111 1982

The ultrastructure and histochemistry of the human urethral mucosa was studied. By scanning electronmicroscopy (SEM) the cover cell of the urethra was found to be polygonal and with a surface topography characterized by numerous microvilli and microridges. By transmission electronmicroscopy (TEM) the cover cells were shown to be interconnected with tight junctions but to lack the asymmetric luminal membrane and the fusiform vacuoles that characterize urothelium above the bladder neck. Histochemical analyses showed the human urethral cells to harbor large amounts of glycogen, and the glycocalyx facing the urethral lumen displayed high affinity for alcian blue and colloidal iron, indicating the presence of acid mucopolysaccharides. The reactivity with alcian blue appeared at pH 2.5, but was abolished by pretreatment with sialidase. Studies with TEM or using SEM with energy-dispersive x-ray spectrometry (EDX) confirmed the high content of acid mucopolysaccharides in the luminal glycocalyx of the cover cells by demonstrating high binding capacity for ruthenium red. The quantitative binding of ruthenium red was not influenced by pH shifts between 4.5 and 7.5. Utilizing the SEM + EDX technique, small variations in quantity of negative charge (ie of bound ruthenium red) were detected within individual cover cells, but considerable variations were found between cells.

The significance of these physicochemical properties of the human urethral lining is discussed with special reference to the previously demonstrated liability of this mucosal surface to interact with microorganisms such as Escherichia coli, Staphylococcus saprophyticus and Neisseria gonorrhoeae. (Author abstract) (37 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

31. HLA ANTIGEN EXPRESSION ON UROTHELIAL CELLS: DETECTION BY ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY.

O'Toole CM, Tiptaft RC, Stevens A
Div. Immunology, Addenbrooke's Hosp., Laboratories Block, Hills Road, Cambridge, CB2 2QQ, England
Int J Cancer; 29(4):391-395 1982

Antibody-dependent cell-mediated cytotoxicity (ADCC) was used to detect HLA-A, -B and -C antigens on in vitro-cultured urothelial cells of normal or malignant derivation. Alloantisera induced specific lysis of 51Cr-labeled targets by effector lymphoid cells from non-immune donors. HLA antisera were routinely titered to dilutions greater than or equal to 10(-3) on urothelial cells in primary or long-term culture. The HLA phenotype was compared for lymphoid cells and urothelial cells from eight individuals. HLA antigens detected by complement mediated lymphocytotoxicity were also detected on urothelial cells. No deletions or gains in HLA antigens were found on normal or malignant urothelial cultures as compared with donor lymphocyte HLA typing. The results show that the established urothelial cell lines J82, TCCSuP and SCaBER have retained their donor HLA phenotype. The established cell lines T24 and RT4 derived from transitional cell carcinomas and HCV-29 from urothelium were found to have distinctive HLA profiles although donor lymphocytes were not available for comparison. The serological crossreactions seen in complement mediated lymphocytotoxicity were clearly observed in ADCC. In particular, HLA-Cw5 was found to crossreact with HLA-Cw8. HLA-Cw5 was detected on 6/8 cultures of transitional cell carcinomas and this was confirmed by absorption analysis. (Author abstract) (19 Refs)

32. CELL-SURFACE A, B, OR H-BLOOD-GROUP ANTIGENS IN UROTHELIAL CANCER.

Newman AJ, Graham MA, Carlton CE
Roy and Lillie Cullen Dept. Urologic Res., Baylor Coll. Medicine, Houston, TX
Cancer Bull; 34(1):7-9 1982

In order to evaluate the prognostic significance of the presence or absence of surface A, B, or H antigens in superficial bladder tumors, a retrospective longitudinal analysis of A, B, or H blood group antigens was performed on 516 bladder tumor specimens collected during the period 1955 to 1972 from patients with Stage A disease. The specific red cell adherence (SRCA) technique was used. A strong correlation was apparent between the presence or absence of A, B, and H group antigens and the propensity for recurrence with invasion in patients with superficial bladder tumors. Only 4% of the patients with lesions initially positive for SRCA subsequently developed invasive lesions, whereas 71% of the patients with initially negative SRCA tests ultimately had invasive cell carcinoma. Of the Grade I and II lesions that were negative for SRCA, 71% became invasive, compared to 75% of the Grade III lesions with initially negative SRCA results. Regardless of the source of tissue containing carcinoma in situ (CIS) or dysplasia (cystectomy specimen for invasive disease or biopsy near a superficial tumor), the vast majority of these areas showed deletion of A, B, or H antigens, indicating that the SRCA reaction has no value in predicting the subsequent clinical course of CIS or dysplasia. Prospective studies of the SRCA test and increased sensitivity for patients with blood type O must be accomplished before established therapies are altered. (13 Refs)

33. STUDIES ON THE IMMUNITY OF PATIENTS WITH UROGENITAL MALIGNANT TUMORS. REPORT 1. EVALUATION OF NONSPECIFIC CELLULAR IMMUNITY BY DELAYED CUTANEOUS HYPERSENSITIVITY TEST AND LYMPHOCYTES BLASTOID FORMATION.

Ono H
Dept. Urology, Shimane Medical Univ., Izumo, Japan
Nippon Hinyokika Gakkai Zasshi; 72(8):1064-1077 1981

Nonspecific cellular immunocompetence was studied in 187 patients with urogenital cancer, 20 with other cancers, 38 with benign prostatic hypertrophy (BPH), and 23 with benign diseases other than BPH. Tests of immunocompetence included skin reactivity to 2-4 dinitrochlorobenzene (DNCB) and purified protein derivative (PPD) and peripheral lymphocyte blast formation induced by phytohemagglutinin (PHA) and pokeweed mitogen (PWM). Urogenital cancers included 97 bladder carcinomas (46 low stage, 21 high stage, 16 disseminated, 14 follow-up), 22 renal cell carcinomas (10 locally advanced, 12 disseminated), 19 pelvic and ureteric carcinomas (8 locally advanced, 11 disseminated), 31 prostatic carcinomas (18 locally advanced, 13 disseminated), and 9 testicular tumors. Patients with advanced urogenital cancers had higher rates of negative responses to DNCB and PPD than those without tumors or with BPH. Compared to patients without tumors or with BPH, those with advanced urogenital tumors had significantly decreased responses to PHA; possibly due to damage of the lymphocytes themselves and inhibition of factors in the serum of the patients with the urogenital cancer. Some decreased response to PWM was observed in the patients with urogenital cancer, but the difference between the cancer and non-cancer groups was not as marked as that seen for PHA. Overall, immunocompetence of cancer patients was decreased compared to that of non-cancer patients. (33 Refs) (In JPN)

34. STUDIES ON IMMUNITY IN PATIENTS WITH UROGENITAL CANCERS. REPORT 2. EFFECT OF ABNORMAL SERUM PROTEINS ON NONSPECIFIC CELLULAR IMMUNITY.

Ono H
Dept. Urology, Shimane Medical Univ., Izumo, Japan
Nippon Hinyokika Gakkai Zasshi; 72(8):1078-1091 1981

Subfraction levels of prealbumin (PA), alpha1-antitrypsin (a1-AT), alpha1-acidglycoprotein (a1-AG), ceruloplasmin (Cp) and haptoglobin (Hp) were measured in the serum of 66 patients with bladder carcinoma, 16 with renal cell carcinoma, 21 with pelvic and ureteric carcinoma, 19 with prostatic carcinoma, 5 with testicular tumor, 15 with other malignancies, 22 with benign prostatic hypertrophy, and 15 with no malignancy. Effects of the serum proteins on nonspecific cellular immunity was studied. Skin response to 2-4 dinitrochlorobenzene (DNCB) and purified protein derivative (PPD) and lympho-

cyte blastogenesis induced by phytohemagglutinin (PHA) and pokeweed mitogen (PWM) were used as indicators of immune response. Alpha1-globulins were significantly increased in patients with metastatic renal carcinoma, pelvic and ureteric carcinoma, or other malignant tumors, and the increases were directly related to the stage of the cancer. High levels of IgG and IgM were observed in the patients with renal cancer but not in other patients. Patients with urinary tract cancers had elevated levels of PA, a1-AG, a1-AT, Cp, and Hp; a1-AT was significantly increased in patients with advanced cancers. Decreased response to PPD was associated with significant decreases in PA and increases in a1-AT, Cp, and Hp. Except for PA and a1-AG, no other serum proteins were associated with changes in DNCB responses. After the addition of autologous serum, PHA-induced blastogenic response was positively correlated with levels of serum PA and negatively correlated with levels of serum a1-AG, a1-AT, and Cp. PWM-induced response was not correlated to levels of serum glycoproteins. The patient's lymphocyte reactivity index was negatively correlated to a1-AT and Cp levels, suggesting suppression of T lymphocyte function by these glycoproteins. (27 Refs) (In JPN)

35. IMMUNOLOGICAL PROFILE OF PATIENTS WITH TRANSITIONAL CELL CARCINOMA OF THE BLADDER.

Mukamel E, Shohat B, Servadio C
(c/o Servadio) Dept. Urology, Beilinson Medical Center, Petah Tiqva, Israel
Br J Urol; 54(1):11-15 1982

The immunological profile of 58 patients with various stages of transitional cell carcinoma of the bladder was determined by using the local xenogeneic graft versus host reaction (GVHR) test, by skin testing with 3 recall antigens (candida, trichophyton, streptokinase-streptodornase) and by quantification of T-lymphocytes. Thirty-two patients with low grade low stage tumors (Group A) showed only a slight impairment of the immunological profile with a slight decrease in T-lymphocytes, 4.4% negative GVHR tests and 31.2% negative skin tests. Ten patients with highly invasive inoperable tumors (Group B) showed a severe impairment of the immunological profile with a significant decrease in T-lymphocytes, 100% negative GVHR and 80% negative skin tests. A marked improvement in the immunological profile was noted while comparing nine patients who were examined within 6 mo after cystectomy (Group CI) (severe decrease in T-lymphocytes 44.4% negative GVHR tests and 66.6% negative skin tests) with seven patients who were examined 18 mo or more after operation (Group CII) (slight decrease in T-lymphocytes 0% negative GVHR and 42.8% negative skin tests). Incubation of T-lymphocytes with a thymic hormone (THF) caused an increase in the extent of the graft versus host reaction in 10 out of 14 patients with low grade low stage bladder tumors. This may represent an improvement in the functional activity of the T-lymphocytes with a possible therapeutic use in the future. (Author abstract) (22 Refs)

36. IMMUNOCHEMICAL STUDY OF ANDROGEN-BINDING BETA-GLOBULIN IN HEALTHY CONTROLS AND CANCER PATIENTS.

Terent'ev AA, Feshchenko SP, Tatarinov IuS
Dept. Biological Chemistry, N. I. Pirogov Second Medical Inst., Moscow, USSR
Biull Eksp Biol Med; 92(1):58-60 1982

Androgen-binding beta-globulin (ABBG) was assayed in blood sera and tissue extracts of healthy controls and cancer patients. Immunodiffusion and immunoelectrophoresis showed the presence of ABBG in extracts of the prostate and the sperm, but not in the blood sera, of the healthy controls. The ABBG was present in tumor tissue extracts of the patients with breast cancer, kidney cancer, stomach cancer, colonic cancer, brain cancer, or testicular cancer and in the blood sera of 50% of the cancer patients. Tests for cross reactions showed that the ABBG was not identical to antigens showing affinity to steroid hormones. (13 Refs) (In RUS)

37. POST-GAMMA GLOBULIN: TISSUE DISTRIBUTION AND PHYSICOCHEMICAL CHARACTERISTICS OF DOG POST-GAMMA GLOBULIN.

Sekine T, Poulik MD
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Clin Chim Acta; 120(2):225-235 1982

Various tissues from three dogs were analyzed by radioimmunoassay for the presence of the low molecular mass protein post-gamma globulin (p-gamma). The mol wt of some reactive extracts was determined by gel filtration. Parotid gland contained the highest amount of p-gamma, and high levels were found in kidney, cerebrospinal fluid, CNS tissue, and serum. The p-gamma in parotid gland, brain, and kidney was the 11 kilodalton (kd) 'free' form, while forms with higher mol wt (approx 27 and 34 kd) were also found in brain and kidney. Extracts of uterus, ovary, and liver, which contain comparatively small amounts of p-gamma, had free and 34 kd material but no detectable 24 kd form. Analysis of three human renal tumors showed that tumor mass contained only the 34 kd form, while normal kidney tissue surrounding the tumor had both 27 and 34 kd forms. (24 Refs)

REVIEWS AND OTHER RELATED STUDIES

38. ADENOCARCINOMA OF THE KIDNEY. A SERIES OF TWO HUNDRED AND THIRTY-SEVEN CASES.

Cinqualbre J, Py JM, Goldschmidt P, Bollack C
Clinique Urologique, Pavillon Chirurgical A, Hopital Central, 1, place de l'Hopital, 67005 Strasbourg Cedex, France
Sem Hop Paris; 58(13):812-814 1982

The authors report on their experience of adenocarcinoma of the kidney. They operated on 237 patients over a period of 10 years. Their results are discussed. They also emphasize the aspects of epidemiology, diagnosis and the therapeutic approach for metastatic diseases. (Author abstract) (8 Refs) (In FRE)

39. GENITO-URINARY MALIGNANCIES.

Paulson DF, Perez CA, Anderson T
Div. Urology, Duke Univ. Medical Center, Durham, NC
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

The epidemiology, natural history, and current treatment of adenocarcinomas of the kidney, transitional cell carcinomas of the renal pelvis, ureter, or bladder, adenocarcinomas of the prostate, squamous cell carcinomas of the penis, and carcinomas of the urethra in males and females are discussed, with particular reference to areas of continuing controversy. (334 Refs)

40. KERATINIZING DESQUAMATIVE SQUAMOUS METAPLASIA OF THE UPPER URINARY TRACT: LEUKOPLAKIA--CHOLESTEATOMA.

Hertle L, Androulakakis P
Dept. Urology, Univ. Mainz Medical Sch., Langenbeckstrasse 1, 6500 Mainz, W. Germany
J Urol; 127(4):631-635 1982

Leukoplakia and cholesteatoma of the upper urinary tract are reviewed, based on reported cases. Emphasis is placed on precise definition of histopathological features of the lesions. Topics include terminology; histopathology; incidence, distribution, and localization; etiology and pathogenesis; symptomatology, diagnosis, and differential diagnosis; keratinizing desquamative squamous metaplasia (KDSM) and urothelial cancer; and management. The designation KDSM is suggested for upper urinary tract pathologies now described as leukoplakia or cholesteatoma. By the proposed criteria, squamous cell carcinoma (SCC) in situ is KDSM with atypia. About 80 patients with KDSM have been reported. The male:female ratio is 3:2, with a peak age at diagnosis of 30-50 yr (only two pediatric patients have been reported). KDSM involves the left kidney slightly more often than the right kidney, and usually arises in the renal pelvis and/or calyces. Urinary calculi are present in about 50% of cases. Recurrences of KDSM after incomplete excision or drug therapy are frequent. No patient with KDSM of the upper urinary tract is known to have progressed to SCC, even after a prolonged clinical course. The recommended treatment of KDSM of the upper urinary tract is conservative surgery, with complete excision of the KDSM plaque and correction of associated conditions predisposing to urinary stasis and infection. (56 Refs)

41. PARANEOPLASTIC ENDOCRINOPATHIES ASSOCIATED WITH NONRENAL GENITOURINARY TUMORS.

Altaffer LF
Dept. Urology, Naval Regional Medical Center, Camp Lejeune, NC
J Urol; 127(3):411-416 1982

The ectopic or inappropriate production of parathyroid hormone (PTH), catecholamines (CTA), serotonin (ST), human chorionic gonadotropin (HCGT), adrenocorticotropic hormone (ACTH), antidiuretic hormone (ADH), calcitonin, estrogens (ES), human placental factor (HPF), erythropoietin, insulin-like substances, and prostaglandins associated with various renal tumors is reviewed. Several case reports of apparent PTH secretion by urothelial tumors exist. In all of the cases resolution of the hypercalcemia followed definite treatment of the cancer. Diagnosis of pheochromocytoma is made by measuring elevated serum, urinary CTA and metabolites. Prognosis is generally good but long-term follow-up with urinary levels of CTA or the metabolites is recommended. Signs and symptoms of some carcinoid tumors are probably caused by excessive production of ST. The secretion of HCGT by testicular neoplasms is well known and the use of HCGT as a tumor marker is applied in practice. ACTH was identified in three cases of carcinoma of the prostate. In 1969, a case of carcinoma of the prostate with evidence of ectopic secretion of ADH by the neoplasm was reported. The secretion of a thyroid stimulating hormone-like substance has been reported in association with trophoblastic tumors in women and in two cases of testis tumors. The secretion of ES, androgens, pregnanediol, and luteinizing hormone, has been associated with Leydig cell tumors, gonadal stromal tumors, and gonadoblastomas. The identification of HPF in the syncytiotrophoblastic cells in malignant teratoma of the testis was reported in 1966. Hypoglycemia has been shown to be associated with a variety of extrapancreatic tumors. Hormonally active tumors frequently demonstrate undifferentiated or anaplastic histologic patterns and, in general, patients with hormonally active tumors appear to have a poor prognosis. (83 Refs)

42. CANCER - PRINCIPLES AND PRACTICE OF ONCOLOGY.

DeVita VT, Hellman S, Rosenberg SA
NCI, Bethesda, MD
Cancer - Principles and Practice of Oncology. Philadelphia, Lippincott, 1926 pp., 1982.

Principles and practices in oncology are reviewed with the aim of presenting an integrated multidisciplinary approach to cancer. Principles of oncology are presented with respect to the cause and evolution of cancer as a biologic phenomenon. The essential principles of modern cancer diagnosis and treatment are discussed, and topics include epidemiology; etiology and prevention of cancer; cell biology and biochemistry; kinetics of cellular proliferation; biology of cancer metastasis; principles of surgical oncology, chemotherapy, and radiotherapy; clinical pharmacology of cancer chemotherapy; design and conduct of clinical trials; diagnosis and staging; and psychosocial aspects of patients with cancer. Practice of oncology is presented with respect to the management of specific cancers and complications caused by either the cancer itself or its treatment. Topics include cancer of the head and neck, stomach, lung, mediastinum, esophagus, pancreas, hepatobiliary system, small intestine, colon and rectum, anal region, genitourinary system, testis, ovary and other gynecologic organs, breast, endocrine system, and skin; sarcomas; cutaneous and intraocular melanomas; tumors of the CNS; childhood cancers; Hodgkin's disease; non-Hodgkin's lymphomas; adult acute leukemias; chronic leukemias; plasma cell neoplasms; paraneoplastic syndromes; management of the patient with an unknown primary site; treatment of metastatic cancer; oncologic emergencies; supportive care; infections; adverse effects of treatment; rehabilitation; administration of cancer treatments; newer methods of cancer treatment; and unproven methods of cancer treatment. (11312 Refs)

43. CELLULAR HETEROCHRONY AND NEOPLASIA.

Pearson RD
Science and Medicine Library, Univ. Toronto, 7 King's College Circle, Toronto, Ontario M5S 1A5, Canada
Med Hypotheses; 8(3):231-235 1982

The concept that 'timing changes' in gene regulation are responsible for malignant transformation and subsequent tumorigenesis is presented. Cells of regenerating rat liver 'retrodifferentiate' (RDF), taking on 'juvenile' or embryonic patterns of antigenic and genetic behavior. RDF is followed by a process of redifferentiation to normal tissue type. Primary malignant cells have often been compared to the invading cells of the trophoblast. Trophoblastic tissue and malignant cells have a number of similarities including their ability to move (metastasize), destroy their host's cells in advance of the invading cells, create a life support system by means of angiogenesis, and subvert their host's immune surveillance and monocyte-macrophage systems. Cellular heterochrony of RDF could explain these similarities. Attempts were made to relate human breast cancer and urogenital cancer to thyroid gland malfunction by showing a higher incidence of cancer in hypothyroidism and a lower incidence in euthyroid and hyperthyroid states. The hormones which render amphibians both neotenic and metamorphic are also possibly responsible for triggering timing changes in the tissues and cells of other metazoans. The observations

that the thyroid hormones thyroxine (T4) and triiodothyronine (T3) enhance rat liver regeneration provide indirect evidence to support this hypothesis. T4 or T3 may act as an anticarcinogen. The use of a polar solvent can induce maturation changes in rhabdomyosarcoma transplantable tumor cells from mice and human colon cancer cells causing the cells to lose a marked degree of malignancy. The cancer cells appear to have metamorphosed and thus relinquished their juvenile or heterochronic behavior. (22 Refs)

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1. TOXICITY AND METABOLISM OF ACRYLONITRILE.
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ORGAN SITE CARCINOGENESIS

Kidney and Urinary Tract

SERIES CK17 No. 82/10 OCTOBER, 1982

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. PRIMARY MALIGNANT RENAL TUMORS IN THE SECOND DECADE OF LIFE: WILMS TUMOR VERSUS RENAL CELL CARCINOMA.

Hartman DS, Davis CJ, Madewell JE, Friedman AC
Div. Genitourinary Radiologic Pathology, Dept. Radiologic Pathology, Armed Forces Inst. Pathology, Washington, DC, 20306
J Urol; 127(5):888-891 1982

Primary renal malignancies occur least frequently in the 2nd decade of life. Of the 4,798 cases of renal cell carcinoma and Wilms tumor referred to the Armed Forces Institute of Pathology 53 renal cell carcinomas and 56 Wilms tumors occurred in the 10 to 20-yr age group. Pathologically, both tumors in this age range are similar to those occurring at the more typical age, and histologic differentiation between renal cell carcinoma and Wilms tumor is seldom a problem. While radiographic evaluation is useful to characterize the neoplasm, evaluate the contralateral kidney and detect the presence of tumor extension, current imaging techniques cannot confidently distinguish these two tumors. (Author abstract) (22 Refs)

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2. EPIDEMIOLOGY OF RENAL TUMORS (MEETING ABSTRACT)

Boufflouz C

Urological Department, University of Liege, Leige, Belgium

Renal and Prostatic Tumours, June 2-12, 1981, Erice, Italy NATO Advanced Study Institute; 1981

Data concerning the incidence rates of renal cancer are presented. Although the epidemiologic features of cancer of the renal pelvis are similar to those of the bladder cancer, rates presented include renal-cell carcinoma since these sites are combined for the usual presentation of incidence and mortality. Renal cancer is nearly two times more frequent in men than in women. Like prostatic cancer, its incidence increases parallel to age. On a world-wide basis, large differences are noticed, rather similar to those observed for prostatic cancer. Very little is known about the risk factors: cigarette smoking, dietary factors (fat), coffee consumption have been suspected. Nephroblastoma (Wilm's Tumor) is a rare childhood tumor, but it is an interesting cancer for the epidemiologist as intra-uterine forms, frequent associations with other tumors or congenital malformations and in some cases, familial aggregations suggest an inherited predisposition and the possibility of mutagens acting in early gestational life. (no Refs)

3. RENAL ONCOCYTOMAS AND THEIR CONGENERS (MEETING ABSTRACT)

Beckman EN, Barnes CA

Department of Pathology, Ochsner Medical Institutions, New Orleans, LA

71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

Since 1979 renal oncocytomas (Onc) have comprised 15 per cent of the lesions resected at our hospital with the clinical diagnosis of renal carcinoma. Four Onc occurred between 1947 and 1978 and six from 1979 to the present. Of the 232 carcinomas since 1947, six have had some of the morphologic features of Onc and, thus, posed potential difficulty in diagnosis. Although the morphologic criteria are not well established for separating Onc from those renal carcinomas with overlapping features, the distinction is crucial because of the potential marked difference in disease course. In contrast to the Onc which, except for one case, were asymptomatic and without hematuria, five of six congeners produced symptoms and two had hematuria. Although all 10 patients with Onc are either living without apparent disease or died without evidence of malignancy, one patient with a congener has had metastasis. Four other patients are being followed. Both Onc and congeners were well-circumscribed tumors, varied considerably in size, lacked papillarity, and were composed of cells with granular pink cytoplasm. Although our Onc had the characteristic central scar, this finding occurred so frequently in congeners and the other renal carcinomas that it was not a useful feature. The congeners lacked the diffuse organoid packeting of cells we found characteristic of Onc. Additional features which in individual cases helped separate the congeners included ballooning of the oncocytic cytoplasm, foci of necrosis, pleomorphism, or clear cells, and yellow-tan, rather than tan-brown, gross color. (no Refs)

4. CASE-CONTROL STUDY OF KIDNEY CANCER (MEETING ABSTRACT)

McLaughlin JK, Mandel JS, Blot WJ, Schuman LM

University of Minnesota, Minneapolis, MN

109th Annual Meeting of the American Public Health Association, November 1-5, 1981, Los Angeles, California. American Public Health Association 390 pp., 1981.

A population based interview case-control study of kidney cancer (renal cell 189.0 and renal pelvis 189.1) was conducted in the 7 county Minneapolis St Paul SMSA (standard metropolitan statistical area). Four hundred and ninety-five cases of renal cell and 74 cases of renal pelvis cancer were interviewed (the largest epidemiologic study to date of these sites). Controls (1190) were selected from population based sources and frequency matched on age and sex to cases. Interview response rates of 98% for cases and 97% for controls were achieved. Because of the exploratory nature of the study, many factors were examined including ethnicity and weight, beverage, diet, smoking, drugs, disease and occupational histories. For renal cell cancer the only ethnic group with an elevated risk was German females. Significantly elevated odds ratios were found for males and females for both renal cell and renal pelvis cancer who smoked cigarettes. Males who consumed diet soda had significantly elevated odds ratios. Other elevated odds ratios have been found for certain drugs, industries and occupational exposures. Indices for Vitamins A, C, fat, total alcohol, cruciferous vegetables, phenacetin and acetaminophen have been developed. (no Refs)

5. RENAL ADENOCARCINOMA IN YOUNG ADULTS (MEETING ABSTRACT)

Schiff M, Herter G, Lytton B

No affiliation given

77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Renal adenocarcinoma is a disease commonly associated with an older population, the median age at the time of diagnosis being approximately 60 years. Recently there has been increased awareness of the occurrence of the identical pathologic entity in children, with some evidence to suggest that their overall survival rate is significantly better than that of an older population with simlar stage disease. We have recently treated a number of young adults, 20 to 40 years of age, with renal adenocarcinoma, and were interested in attempting to determine whether the seemingly improved survival data noted in the pediatric population extended beyond the first two decades of life, and if so, whether this was due to differences in the natural history of the disease itself or simply to the lack of intercurrent disease in the younger population. We therefore reviewed 523 cases of renal adenocarcinoma which were seen at our institution between 1948-1980 and found that 37 of them (7.1%) were inpatients 40 years or less at the time of diagnosis. Survival data for this group of young adults was compared with the remainder of the group (above 40 yrs), for similar stage of disease. Patient survival at 3, 5, and 10 year intervals was distinctly better for the younger age group, for both Stage I as well as Stage II and III disease; survival in Stage IV disease was uniformly poor. Further analysis of the data revealed that the improved survival in the younger group could not be attributed to a greater number of non-cancer deaths in the older population; the percentage of patients who died without evidence of disease was essentially identical in the two groups. (no Refs)

6. TRANSITIONAL CELL CARCINOMA OF THE BLADDER IN CHILDREN (MEETING ABSTRACT)

Andriole GL, Lack E, Bauer SB, Colodny AH, Retik AB

No affiliation given

77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Similar to adult urothelial tumors, the most common presentation in childhood is painless gross hematuria (70%). The male predilection (9:1) in children is more marked than that seen in adults, as is the propensity of these tumors to be low-grade, papillary, unifocal, and non-invasive (90%). The natural history of these tumors further contrasts with the adult experience in that recurrence after initial resection is very unusual (less than 5%). In considering the pathobiology of these childhood tumors, it is important to distinguish benign 'papilloma' from malignant 'papillary transitional carcinoma'. Only the latter growths display atypical epithelium, and clinically, they tend to recur and invade, whereas papillomas don't. The observed similarity in the behavior of papillomas and reported childhood papillary tumors raises the possibility that some of the reported cases, particularly those with ambiguous histopathology, may in fact represent papillomas rather than carcinomas. Hence, the incidence of true papillary transitional cell carcinoma in children may be even lower than heretofore expected. The surgical management of these childhood urothelial tumors has varied from transurethral resection, to suprapubic, transvesical excision, and in some cases, to partial cystectomy. Experience with those cases with adequate follow-up suggests that any method which assures total resection of the primary tumor with minimal morbidity is appropriate. (no Refs)

7. THE RISK OF UPPER URINARY TRACT TUMOR IN PATIENTS WITH BLADDER CARCINOMA (MEETING ABSTRACT)

Mechali P, Correa RJ

No affiliation given

77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

It is a prevalent opinion that patients with bladder tumors (BT) are at high risk for developing transitional cell upper urinary tract tumors (UTT). As a corollary, it is an accepted practice to do repeated routine IVP to monitor for the appearance of such tumors. We undertook the current study in order to test the validity of that approach. First, we analyzed the charts of 382 patients referred to the Mason Clinic for bladder tumor, between 1943 and 1971, and followed up for 10 years or more, or until their death. BT preceded UTT concomitant 1/382-BT and UTT concomitant 1/382. BT occurred after UTT was diagnosed: 7/382. No UTT 373/382. Second, we looked at 52 patients referred to the Mason Clinic for upper urinary tract transitional cell tumors between 1943 and 1981, an overlapping but not identical population: BT before UTT: 2/52-BT and UTT concomitant 5/52 (one subsequently recurred) - BT after UTT: 12/52. No BT 33/52. The incidence of 3.8% of UTT preceded by BT is impressive, but one has to observe that this reflects the referral bias of a large institution (which is more likely to publish and set trends in the practice of urology). On the other hand, only .26% of BT were found to be followed by UTT. This suggests that in unselected BT, it may not be indicated to do repeated routine IVP in otherwise asymptomatic patients to screen for UTT. (no Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

8. ARTIFICIAL SWEETENERS AND BLADDER CANCER IN MANCHESTER, U.K., AND NAGOYA, JAPAN.

Morrison AS, Verhoek WG, Leck I, Aoki K, Ohno Y, Obata K
Dept. Epidemiology, Harvard Sch. Public Health, Boston, MA
Br J Cancer; 45(3):332-336 1982

We have evaluated the relation between cancer of the lower urinary tract ('bladder cancer') and the use of artificial sweetners, by means of case-control studies in Manchester, UK, and Nagoya, Japan, areas where extensive use occurred 30-40 yr ago. In each area, a broadly based series of cases (555 in Manchester, 293 in Nagoya) was interviewed and a series of controls (735 in Manchester, 589 in Nagoya) chosen from the general population. A history of use of sugar substitutes primarily saccharin, was not associated with an elevated risk of bladder cancer in either study area. Risk of bladder cancer did not increase regularly with frequency or duration of use of sugar substitutes. Data on dietetic beverages were not obtained in Nagoya. This exposure was not associated with a greater risk of bladder cancer in Manchester. The results of this study suggest that use of artificial sweetners confers little or no risk of bladder cancer. (Author abstract) (10 Refs)

9. INTRA-UTERINE EXPOSURE TO SACCHARINE AND RISK OF BLADDER CANCER IN MAN.

Jensen OM, Kamby C
Danish Cancer Registry, Strandboulevarden 49, DK-2100 Copenhagen 0, Denmark
Int J Cancer; 29(5):507-509 1982

Animal experiments show that rats fed saccharine are more likely to develop bladder tumors if they have been exposed to saccharine in utero through their mothers' food. The risk of bladder tumors in humans following in utero exposure to saccharine has not been evaluated previously. In Denmark the use of saccharine increased sharply during the second World War as a result of scarcity of sugar, and import and export figures indicate that saccharine consumption was on av 4-5x higher during the war-time period than the pre-war decade. The risk of bladder tumors at ages 20-34 was 1.0 (95% confidence interval 0.7-1.6) among men born in 1941-1945 compared with men born 1931-1940. Among women the risk was 0.3 (0.1-1.0). This study provides no evidence of an increased risk of human bladder cancer during the first 30-35 yr of life associated with in utero saccharine exposure. (Author abstract) (20 Refs)

10. PREDICTIVE IDENTIFICATION OF HYPERSUSCEPTIBLE INDIVIDUALS.

Omenn GS
Dept. Environmental Health, Univ. Washington, Seattle, WA, 98195
JOM; 24(5):369-374 1982

Genetic traits that may predispose individuals to occupational diseases are reviewed. A single-gene difference affecting N-acetyl-transferase (NAT) activity in liver makes individuals slow acetylators (recessive) or rapid acetylators (dominant) of a series of clinically important drugs. NAT is known to be involved in acetylation and thus inactivation arylamines that are potent bladder carcinogens, including beta-naphthylamine, benzidine, 4-amino-biphenyl, and 4-nitrobiphenyl, all of which are used as industrial oxidants. An excess of slow acetylators has been observed in groups with a high incidence of occupational

bladder cancers. Genetic control of microsomal oxidizing systems appears to be related to certain occupational disease. Aryl hydrocarbon hydroxylase (AHH) has been shown to be involved in activating many promutagenic and procarcinogenic aryl hydrocarbons, of which benzopyrene is the prototype. The pesticide parathion and its active metabolite paraoxon are inactivated by plasma paraoxonase. Potential genetic predispositions due to differences in tissue sensitivity include the following: hemolysis due to glucose-6-phosphodiesterase; sickle cell trait; plasma alpha-antitrypsin deficiency and pulmonary emphysema; low-back pain, ankylosing spondylitis, and histocompatibility antigen B27; and skin hypersensitivity reactions. Opportunities for research/criteria for development of screening tests are discussed. (35 Refs)

11. EPIDEMIOLOGY OF INDUSTRIAL BLADDER CANCER IN WEST YORKSHIRE (MEETING ABSTRACT)

Cartwright RA, Glashan RW

Yorkshire Regional Cancer Organization, Cookridge Hospital, Leeds, England

Br J Cancer; 44(2):277 1981

This paper presents some preliminary results from a case-control study currently underway in parts of West Yorkshire. To date 1015 cases and 1288 controls have been analyzed. Of these 72 cases and 37 controls were employed for at least 6 months in the chemical industry, giving a maximum-likelihood estimation of the risk ratio as 3.1 (95% confidence limits of 1.9-3.8). Other trades whose work brought them into contact with the chemical industry have an excess of bladder cancer cases among them, at a ratio of 2.5. Process workers associated with the dye-manufacturing industry, who form a substantial proportion of chemical workers, have a higher risk still of bladder cancer (4.5). The case-control interviewing approach of this study makes it possible to estimate how other determinants of bladder cancer influence the risks for such hazardous occupations. Process workers who smoke have a risk ratio of nearly 6 while non-smoking process workers have a lower and statistically insignificant risk. (no Refs)

12. LIFETIME OCCUPATIONAL AND BLADDER CANCER (MEETING ABSTRACT)

Najem GR, Louria DB, Thind IS, Seebode JJ

New Jersey Medical School, Newark, NJ

109th Annual Meeting of the American Public Health Association, November 1-5, 1981, Los Angeles, California. American Public Health Association 390 pp., 1981.

The present case-control study of bladder cancer in two northern counties of New Jersey was conducted to investigate a tumor that has been considered to have a strong association with industrial and environmental exposures. The study population included 75 bladder cancer cases and 150 matched controls. Cases and controls were matched for race, sex, age, place of birth, and place of residence. Risk ratios of greater than 2.0 were found for cigarette smoking among male and female cases and for working in dye, petroleum (fuel), or plastic industries among male cases. No significant association was found for: cigar and pipe smoking; caffeine, saccharine, and alcohol consumption; use of hair dyes, and lifetime occupational history of working in other than dye, petroleum, and plastic industries. No differences were found in family history of cancer. Simultaneous multiple primary cancer sites were found in 9.3% of the bladder cancer patients; this is higher than the 0.2 to 8% reported in the medical literature. (no Refs)

13. EPIDEMIOLOGIC SURVEY OF BLADDER CANCER IN GREATER NEW ORLEANS (MEETING ABSTRACT)

Sullivan JW

No affiliation given

77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The primary ancestry of the cases and the controls was not statistically different, but the Jewish population had a significantly greater increased incidence of bladder cancer. Overall, a significantly greater number of cases smoked filtered cigarettes, commenced consumption of artifical sweetened beverages at an ealier age, drank artificial sweetened beverages for a greater number of years, consumed a greater number of glasses of artificial sweetened beverages per week and related a history of urinary tract infections. A significantly increased incidence of bladder cancer was noted in individuals employed by certain types of companies, by certain job titles, and by certain job material handled. Analysis of the data failed to show any significant difference in years of consumption of coffee, amount of various types of coffee or tea consumed, consumption of various alcoholic and non-alcoholic beverages including source of drinking water, usage of hair dye, incidence of diabetes mellitus, family history of urinary cancer, history of pelvic irradiation or bladder stones. (no Refs)

14. CANCER ASSOCIATED WITH ASBESTOSIS, SCHISTOSOMIASIS, FOREIGN BODIES, AND SCARS.

Brand KG

Dept. Microbiology, Univ. Minnesota Medical Sch., Minneapolis, MN

Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

An etiologic connection between asbestosis and cancer can no longer be disputed. One out of five asbestos workers dies from cancer of the lung. In another 10% the pleura, peritoneum, larynx, pharynx, or the alimentary tract is afflicted. The time of latency from first exposure until detection of the cancer is between 20 and 40 yr. A causal relationship between Schistosoma haematobium infection and cancer of the urinary bladder is indicated by several pieces of evidence. The incidence of bladder cancer in schistosomiasis patients peaks between the ages of 30 and 50 yr, whereas bladder cancer without underlying schistosomiasis is rarely encountered before the age of 50. Both asbestos and schistosomiasis cancers have pointed to tissue as a circumstance conspicuously linked to preneoplastic development. This association is further strengthened by numerous reports of scar-related cancer. After latencies of several decades, sarcomas were seen to arise from scars caused by bullet wounds, surgical operations, or amputations. Carcinomas, frequently of the epidermoid type, developed from deep burn scars and chronic fistulas of the bone. Nondegradable foreign bodies acquired by accident or implanted for medical reasons cause chronic tissue reactions that are characterized by scar-like fibrotic encapsulation of the foreign bodies. Such conditions can lead to neoplasms in humans and animals. (102 Refs)

15. CHILDHOOD TYPE RENAL MEDULLARY CYSTIC DISEASE.

Shi Y, Li G
Dept. Pediatrics, Third Teaching Hosp., China Medical Coll., Shenyang, People's Republic of China
Zhonghua Erke Zazhi; 19(3):157-159 1981

Childhood type renal medullary cystic disease (MCD), also known as familial juvenile nephrophthisis, is a rare hereditary progressive kidney disease. Clinical and pathological findings are described for four cases (1 male, 3 females; 5-11 yr old) from three families. Pathological findings of two of the cases are detailed and the three family histories are given. (9 Refs) (In CHI)

16. OCCUPATION AS AN ETIOLOGIC FACTOR IN RENAL CELL CARCINOMA (MEETING ABSTRACT)

Asal NR, Bryan JS, Geyer JR
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

This study was designed to investigate the significance of occupation as an etiologic factor in renal cell carcinoma. Two hundred patients with this diagnosis, who were hospitalizd in Oklahoma City and Tulsa between 1977 and 1980, were matched with 400 controls according to age, sex, race and hospital. Data was collected from hospital records and from questionnaires which were mailed to the living patients, controls (both hospital and general population) and next of kin of the deceased individuals. In addition to the occupational history, other risk factors were analyzed such as family history of cancer, smoking, alcohol consumption, use of hormones, previous illness and radiation therapy. The incidence of renal cell carcinoma was higher than expected in several occupations, including dry cleaners, truck drivers, welders/plumbers and physicians/dentists. There were five dry cleaners among the cases compared to none in the controls. Also 12% of the cases and 5% of the controls responding to the questionnaire were truck drivers. (no Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

17. INDUCTION OF BLADDER CANCER IN RATS BY FRACTIONATED INTRAVESICULAR DOSES ON N-METHYL-N-NITROSOUREA.

Severs NJ, Barnes SH, Wright R, Hicks RM
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Br J Cancer; 45(3):337-351 1982

Experiments were conducted to determine the dose response of rat bladder urothelium to a range of different single and fractionated intravesicular doses of the carcinogen, N-methyl-N-nitrosourea (MNU). A dose-related response of bladder-tumor incidence to single graded doses of MNU was found, and a threshold dose suitable for use in multistage carcinogenesis experiments was derived from these data. For any given total dose of MNU, the tumor incidence was greater if the MNU had been administered in several small fractions than if it had been administered in fewer larger ones. Extending the interval between doses did not reduce the tumor incidence. It is argued that these results support the multistage theory of carcinogenesis. The histopathology and cell-surface alterations which characterize the development of MNU-induced bladder cancer are described and the contribution of hyperplasia and calculi are discussed. (Author abstract) (39 Refs)

18. COCARCINOGENICITY OF SACCHARIN TOWARD N-DIBUTYL-NITROSAMINE CARCINOGENICITY IN RAT LIVER AND URINARY BLADDER (MEETING ABSTRACT)

Pereira MA, Britt AL
Health Effects Research Laboratory, US Environmental Protection Agency, Cincinnati, OH
Toxicologist; 2(1):64 1982

Saccharin has been demonstrated to be a promoter of chemical carcinogenesis in the rat urinary bladder. Since other tumor promoters are also cocarcinogens, we evaluated the possibility that saccharin is also a cocarcinogen. Male Fisher 344 rats simultaneously received 0.02% dibutylnitrosamine (DBN) in their drinking water and 5% sodium saccharin in their diet for a total of 26 weeks. The liver of rats that received only DBN contained 16 hyperplastic nodules among 5 of 29 (17%) animals and 2 hepatocellular carcinomas in 1 of 29 (3%) of the animals. The simultaneous administration of sodium saccharin to the animals that received DBN, produced an enhanced hepatocarcinogenic response of 106 hyperplastic nodules in 17 of 21 (81%) animals and 81 hepatocellular carcinomas in 17 of 21 (81%) animals. The number of preneoplastic focal alterations in the liver that were induced by DBN, was also enhanced by sodium saccharin. The livers of untreated control rats an rats that received only sodium saccharin were free of preneoplastic foci, hyperplastic nodules and hepatocellular carcinomas. In the urinary bladder, treatment with DBN produced simple and nodule hyperplasia that was enhanced by simultaneous treatment with saccharin. Sodium saccharin did not result in either a preneoplastic hyperplasia or a neoplastic response in the urinary bladder of the rats. (no Refs)

19. MUTAGENICITY, CARCINOGENICITY, AND BIOCHEMICAL ACTIVITY OF ELEVEN NEW 5-NITROFURAN ANALOGS (MEETING ABSTRACT)

Erturk E, Swaminathan S, Ichikawa M, Bryan GT
University of Wisconsin Center for Health Sciences, Madison, WI, 53792
Fed Proc; 41(3):330 1982

New analogs of the bladder carcinogen N-[4-(5-nitro-2-furyl)-2-thiazolyl]formamide, (FANFT), were synthesized and tested for antibacterial activity against Esherichia Coli and Staphylococcus Aureus, and for mutagenicity against Salmonella TA-100 (Ames test). Two compounds were further tested for their ability to induce ornithine decarboxylase (ODC) in the urinary bladder, and for their carcinogenicity in female rats after 46 wks of exposure in diet followed by 20 wks of control feed. The test compounds were: 2-formylamino-4-[2-(5-nitro-2-furyl)vinyl]-1,3-thiazole (I), 2-amino-4-[2-(5-nitro-2-furyl)vinyl]-1,3-thiazole (II), 5-nitro-3,4-diphenyl-2-methyl furoate (III), 5-hydroxylamino-3,4-diphenyl-2-methyl furoate (IV), 5-amino-3,4-diphenyl-2-methyl furoate (V), methyl(2-oxy-3,4-diphenyl-4-cyano)butanoate (VI), methyl(2-oxy-3,4-diphenyl-4-cyano)butenoate (VII), 2,5-dioxy-3,4-diphenyl-3-pyrroline (VIII), 5-(N-acetylamino)-3,4-diphenyl-2-methyl furoate (IX), 5-(N,N-diacetylamino)-3,4-diphenyl-2-methyl furoate (X), and 5-(N-acetylamino)-2-(2-thiazolyl) furane (XI). I and II, the vinyl bridged analogs of FANFT, showed antibacterial activity against both bacteria, were mutagenic to TA-100, and induced urinary bladder ODC; however, they were not carcinogenic in

rats. III was antibacterial and mutagenic, and other analogs were neither antibacterial nor mutagenic. (no Refs)

20. INDUCTION OF RENAL CELL TUMORS IN F344 RATS BY ORAL ADMINISTRATION OF POTASSIUM BROMATE, A FOOD ADDITIVE.

Kurokawa Y, Hayashi Y, Maekawa A, Takahashi M, Kokubo T
Div. Pathology, Natl. Inst. Hygienic Sciences, Kamiyoga 1-18-1, Setagaya-ku, Tokyo 158, Japan
Gan; 73(2):335-338 1982

Carcinogenicity of potassium bromate (K bromate) was studied in F344 rats administered K bromate (500 or 250 ppm) po in distilled water for about 2 yr. In males treated with 500 ppm, the concentration was reduced to 400 ppm at wk 60 due to inhibition of body wt increase. Control rats were given distilled water only, and each dose group consisted of 53 male and 53 female rats. Treatment with K bromate was terminated wk 110, and all surviving animals were sacrificed at wk 111 and examined. Most kidneys were sectioned in 10-15 slices 4 micrometer thick, and examined with hematoxylin and eosin stain. Mean survival time (88.1 +-18.2 wk) was shortest in males given 500 ppm K bromate; survival times of other groups were between 101-104 wk. Survival ratios at wk 104 were relatively high in the female rats treated with the K bromate. The first renal cell tumor was observed in a male rat which died wk 14; mean induction time for renal cell tumors ranged from 90 wk in males treated with 500 ppm K bromate to 111 wk in control male rats. Incidences of renal cell tumors in male rats were 90.4% (500 ppm), 58.5% (250 ppm), and 5.7% (controls); those in female rats were 69.2% (500 ppm), 50.0% (250 mm), and 0% (controls). The values for the test groups were all significantly different than those for controls. Microscopically, the renal cell tumors were adenomas or adenocarcinomas. More than 80% of the tumors were classified adenocarcinomas. Often, both adenomas and adenocarcinomas were observed in the same rat. The results indicate that po K bromate induces renal cell tumors in both male and female F344 rats and that the incidences were dose-dependent. (14 Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

21. PROTECTIVE EFFECT OF NICOTINAMIDE ON BRACKEN FERN INDUCED CARCINOGENICITY IN RATS.

Pamukcu AM, Mulli U, Bryan GT
Div. Clinical Oncology, Dept. Human Oncology, Wisconsin Clinical Cancer Center, K4/554, CSC, 600 Highland Ave., Madison, WI, 53792
Nutr Cancer; 3(2):86-93 1981

Albino noninbred weanling male and female rats were fed a basic grain diet (Group 1), a basic diet supplemented with 0.5% nicotinamide (Group 2), a basic diet containing 33% bracken fern (BF) (Group 3), or a basic diet supplemented with 33% BF and 0.5% nicotinamide (Group 4) for 58 wk. Dietary nicotinamide decreased the BF-induced incidence of both intestinal and bladder tumorigenesis by about 40%. The inhibitory effect of nicotinamide on the BF-induced intestinal and bladder tumors was significant at p less than 0.05 and p less than 0.01, respectively. (Author abstract) (39 Refs)

22. PROTECTIVE EFFECTS OF BLADDER SURFACE GLYCOSAMINOGLYCANS AGAINST CARCINOGENIC AGENTS (MEETING ABSTRACT)

Bodenstab W, Stauffer C, Schmidt JD, Parsons CL
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association Missouri. American Urological Association 254 pp., 1982.

It has been shown in animal models that the bladder surface is lined by a layer of glycosaminoglycans (GAGs) that prevents bacterial adherence and infection. The GAG layer also prevents calcium and proteins from adhering to the bladder surface. We believe that GAG layer acts as a nonspecific barrier between the transitional cells and the environment, protecting them from infection, stone formation and carcinogenesis. To determine whether the GAG layer also blocks the access of carcinogens to the transitional cells we tested the tumorigenic effects of methylnitrosourea (MNU), a complete carcinogen, in 4 groups of rabbits using an in vivo assay that we have described. Group 1 received MNU only; Group 2 underwent removal of the natural GAG layer with HCl followed by treatment with MNU; Group 3 underwent HCl removal of the GAG layer and its replacement with the synthetic analog sodium pentosanpolysulfate (SP54) followed by treatment with MNU; Group 4 received SP54 followed by MNU. All rabbits' bladders were assayed for tumors at 18, 22, 26, 30 and 34 weeks. Group 2 showed the highest incidence of tumors, approximately 55%. Approximately 25% of Group 1 rabbits, 12% of Group 3 rabbits and 6% of Group 4 rabbits developed tumors. The differences between tumor incidence in the groups receiving SP54 before MNU (Groups 3 and 4) and the group receiving MNU after HCl removal of the natural GAG layer (Group 2) were statistically significant, suggesting that SP54 prevented the increased carcinogenic effects of MNU seen in bladders whose natural GAG layer had been removed. (no Refs)

23. EXPERIMENTAL STUDY OF THE BIOLOGICAL EFFECTS OF SMALL CONCENTRATIONS OF A MIXTURE OF DIMETHYLNITROSAMINE, DIMETHYLAMINE, AND NITROGEN DIOXIDE.

Prusakov VM, Benemanskii VV, Leshchenko ME, Katul'skii IuN
No affiliation given
Gig Sanit; (3):8-11 1982

The carcinogenic effect of combined exposure to a mixture of dimethylnitrosamine (DMNA), dimethylamine (DMA), and nitrogen dioxide (NDO) was studied in random-bred albino rats. The animals were subjected to a chronic, around-the-clock inhalation exposure to DMNA alone (0.07-0.66 mg/cubic meter) or in combination with DMA and NDO. The experiment continued for 1 yr. Analysis of the toxic effects DMNA alone and in combination with DMA and NDO showed wave-like changes in the RBC, WBC, and platelet counts. Exposure to DMNA resulted in a dose-dependent increase of liver and kidney tumors. Significant increase of the tumor yield after exposure to DMNA alone was observed for the doses of 19.2-44.2 mg/rat. DMNA in combination with DMA and NDO induced tumors at doses of 3.9-16.7 mg/rats. These findings are indicative of the synergism between DMNA, DMA, and NDO with respect to the carcinogenic activity and additive effect with respect to the general toxicity. (3 Refs) (In RUS)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

24. ANDROGEN REGULATION OF DMN-N-DEMETHYLASE ACTIVITY IN KIDNEY OF BALB/C MICE (MEETING ABSTRACT)

Mohla S, Ahir S, Ampy FR
Department of Oncology, Howard University College of Medicine, Washington, DC, 20060
Med Pediatr Oncol; 10(1):102 1982

Androgenic hormones have been shown to regulate the biotransformation of dimethylnitrosamine (DMN) to its active mutagenic metabolite. This androgenic regulation in renal tissue is a receptor mediated phenomenon as androgens are not able to stimulate kidney microsomal enzymes required for Ames test, in Tfm mice. Further, even though hepatic emzymes are more active than the kidney enzymes, the androgen effect is tissue (kidney) specific. Recent observation indicates that this androgenic effect is observed only under conditions when androgen receptors are translocated in the nucleus. The present experiments were designed to test correlations between the mutagenic ability of renal tissue and its N-demethylase activity (an enzyme implicated in conversion of DMN to its active metabolite). N-demethylase activity was measured from micromosomal fractions of liver and kidney (by quantitating formaldehyde formation) according to Nash. The results indicate: (1) higher DMN-N-demethylase activity in liver (male or female, adults) compared to kidney (male or female); (2) higher enzyme activity in adult male compared to adult female renal tissue; (3) complete loss of renal but not liver enzyme activity in mice castrated for 7 days (testosterone treatment, 2 mg/day/10 days, can significantly increase enzyme activity of kidney tissues in such castrates); and (4) a significant increase in DMN-N-demethylase activity in renal tissue of testosterone treated adult female mice. These data indicate androgenic regulation in kidney DMN-N-demethylase activity. The BALB/c mouse kidney system is a useful model to study the mechanism(s) by which steroid hormones augment or inhibit biotransformation of procarcinogens to mutagens which may ultimately lead to tumorigenesis. (2 Refs)

25. NUCLEAR ESTROGEN BINDING IN HORMONALLY AND NON-HORMONALLY INDUCED RENAL CARCINOMA (MEETING ABSTRACT)

Sufrin G, Alvarez J, Swaneck G
No affiliation given
77th Annual Meeting of the American Urological Association, Inc; May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Animal models of Renal Carcinoma (RC) have been described and the estrogen induced RC of the hamster is a unique example of a hormonally induced and hormonally dependent neoplasm. Since a critical requirement of estrogen responsive tissue is estrogen binding to their nuclei, we studied nuclear estrogen binding in this tumor and in RC induced in rats by the non-hormonal drug streptozotocin. RC was obtained from male hamsters after continuous (8-10 months) treatment with diethylstilbestrol (DES) (total dose, 300mg) and from male Wistar Furth rats 9-11 months following a single injection of streptozotocin (65 mg/kg). Purified renal nuclei were isolated and nuclear estrogen binding measured using a tritiated estradiol (3HE2, 98Ci/mmol) exchange assay. Specific binding was determined by subtracting total from non-specific binding. Saturation analysis of hamsters RC nuclei showed a 6-10 fold increase in the amount of 3HE2 specifically bound as compared to nuclei from untreated animals. In contrast, no increase 3HE2 binding was observed when abdominal muscle nuclei or liver nuclei from DES treated animals were compared to muscle or liver nuclei from untreated controls. The amount of 3HE2 bound by nuclei from streptozotocin induced RC showed no change as compared to untreated controls. Moreover when renal nuclei from Wistar Furth rats who were treated with DES for 8 months and who do not develop RC in response to chronic DES were compared to untreated controls, no change in 3HE2 binding was noted. The estrogen induced and estrogen dependent hamster RC exhibits binding characteristics associated with estrogen target tissue and with other estrogen dependent tumors. (no Refs)

26. INVESTIGATION OF PURINE METABOLIC IMBALANCE ON EXPERIMENTAL AND HUMAN KIDNEY TUMORS (MEETING ABSTRACT)

Prajda N, Weber G, Kopper L, Lapis K, Eckhardt S
National Institute of Oncology, Budapest, Hungary
VI Meeting of the European Association for Cancer Research, October 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

There is no effective chemotherapy against human renal cell carcinomas. Elucidating the enzymic programs of these solid tumors should throw light on the metabolic basis of the problems in clinical treatment. The activity of the rate-limiting enzyme of purine biosynthesis amidotranferase (EC 2.4.14) and catabolism, xanthine oxidase (EC 1.2.3.2) was measured in primary human renal cell carcinomas and in chemically induced transplantable renal cell carcinomas of the rat. Enzyme activities were measured in the supernatant by fluorimetric and spectrophotometric methods. In human and rat tumors the activities of amidotransferase increased 1.5-2.7-fold whereas that of xanthine oxidase decreased to 25-69% of control values. We observed an inhibitory effect of glutamine analogs (Azaserine, Acivicin) on the amidotransferase activity in both tissues. Antiglutamine agents might have a role in the chemotherapy of kidney tumors. (no Refs)

27. THE PRESENCE OF RETINOIC ACID RECEPTOR IN HUMAN BLADDER TUMOURS (MEETING ABSTRACT)

Fagg SL, Hughes A, Dawson-Edwards P, Hughes MA
Department of Surgical Immunology, Medicine and Urology, Queen Elizabeth Hospital, Birmingham, England
Br J Cancer; 44(2):309 1981

Specific intracellular receptors for retinoic acid (RAR), analogous to receptors for steroid hormones, are found in a variety of malignant tissues including human lung, breast, cervical, endometrial and ovarian tumors. There is no previous report of RAR in bladder tumors. In this study RAR was measured in human bladder tumor specimens obtained by transurethral resection. Tumor specimens were frozen in liquid N2, and pulverized with a Mikro-Dismembrator. The powder was suspended in 4 vols (w/v) of cold buffer (10 mM Tris, 1.5 mM EDTA, 10 mM DTT, 1.4 M glycerol pH 7.4) and cytosol prepared by high-speed contrifugation (240,000 gx 1 1/2 h). Specific binding was assessed using an agarose-gel electrophoresis system, following incubation with labelled RNA retinoic acid (RA) (40 Ci/mmol) together with the appropriate controls containing an excess of unlabelled RA. Retinol did not compete in this system nor was there any specific binding of RA in serum. RAR was detectable in the cytosols of 6 specimens (ranging from 0.15-1.13 pmol RA/mg cytosol protein). There was no detectable RAR in 3 specimens. These results suggest that RA and its synthetic analogues may be useful in the treat-

ment of some bladder tumors. This study is continuing, and will be combined with a clinical trial using retinoids in the treatment of patients with bladder tumors. (no Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

28. HISTOPATHOLOGICAL STUDY ON CARCINOMA OF THE URINARY BLADDER. 1. THE CLINICAL SIGNIFICANCE OF ITS STROMAL REACTION.

Iseki T, Yamamoto K, Nishio S, Maekawa M, Yasumoto R, Matsumura T, Tsujita M
Dept. Urology, Osaka City Univ. Medical Sch., Osaka, Japan
Nippon Hinyokika Gakkai Zasshi; 72(9):1138-1144 1981

Histological features of tumors and clinical significance of stromal reactions were studied in 50 patients (40 men, 10 women, 47-72 yr old) with carcinoma of the urinary bladder. The carcinomas included 41 transitional cell, 2 squamous cell, 5 adenocarcinomas, and 2 undifferentiated type. Stromal reaction was evaluated based on cellular reaction (4 group classification system of lymphocytic infiltration by Sarma), and fibrous reaction (5 group classification system by Hanabusa), and the correlations between stromal reaction and tissue growth pattern, depth of infiltration, prognosis, tumor grade, and mode of invasion were investigated. A significant correlation was observed between stromal reaction and tumor growth pattern (p less than 0.05), depth of infiltration (p less than 0.025), and mode of invasion (p less than 0.025). Tumor grade was not correlated with stromal reaction. Judging cellular reaction based on lymphocytes, neutrophils, plasmacytes, etc, a significant correlation was observed between the number of neutrophils and depth of tumor invasion but not between any other parameters. Presence and absence of cellular or fibrous stromal reactions was related to prognosis in in 34 patients who were followed-up. (28 Refs) (In JPN)

29. CYTOLOGIC AND HISTOLOGIC FEATURES OF MIXED CARCINOMA OF THE URINARY BLADDER (MEETING ABSTRACT)

Mandell D, Rosenthal DL, Waisman J
Division of Surgical Pathology, University of California, Los Angeles, CA
Acta Cytol (Baltimore); 25(6):717 1981

Five cases of mixed carcinomas of the urinary bladder, each with a mixed population of malignant appearing transitional and glandular cells in the urine and urinary washings, are presented. We defined mixed carcinomas as having major, distinct and simultaneous neoplastic transitional, glandular or squamous components; we did not include minor metaplastic elements in this group. Most cancers of the urinary bladder are transitional carcinomas, with a varied population of transitional cells in urine and washings of the urinary bladder. Poorly differentiated transitional carcinomas frequently have small areas of squamous and glandular metaplasia, but the cells in the urine and urinary washings reflect the anaplastic character of the tumor, and the minor metaplastic components do not represent a diagnostic problem. Likewise, the pure adenocarcinomas and epidermoid carcinomas of the bladder are readily identified by the presence of large numbers of atypical cells of characteristic differentiation in the urine and in vesical washings. All five of our mixed carcinomas were mixed transitional and adenocarcinomas. The histology and cytology of these tumors contrasted with those from unmixed carcinomas of the bladder having squamous and glandular metaplastic components. (no Refs)

30. ULTRASTRUCTURAL STUDIES OF BLADDER BIOPSIES IN PATIENTS WITH RECURRING PAPILLARY TUMOURS (MEETING ABSTRACT)

Smith AF
Institute of Urology, London WC2, England
VI Meeting of the European Association for Cancer Research, October 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

The mucosa of the bladder from patients who have recurring tumors is very varied, sometimes showing areas of atypia, hyperplasia or carcinoma in situ in addition to apparently normal tissues. We examined such cystoscopically normal areas from 8 patients with recurrent tumors and compared them with biopsies taken from 7 patients having no history of neoplasias. Resin embedded material was examined with both the light and electron microscope. When seen with the light microscope, 5u, toluidine-blue stained sections from tumor patients showed small, dark cells among normal superficial ones, whose frequency was significantly higher than in controls. These are incompletely matured superficial cells and their ultrastructure confirms this. They lack the characteristic asymmetric unit membrane and often have microvilli on their surface. Often they show abnormal junctional complexes, with the zonula occludens attenuated or absent. The frequency of abnormal junctions is also significantly higher in tissues from tumor patients than in controls. The inability of the cells to complete maturation may be due to a genetic abnormality or to abnormal metabolites or carcinogens present in the urine. These cellular deficiencies may reduce the protection which normal superficial cells provide and expose the underlying tissues and blood vessels to the potentially harmful effects of substances present in the urine and so increase the likelihood of recurrence of tumors. (no Refs)

31. CYSTIC PARTIALLY DIFFERENTIATED NEPHROBLASTOMA (MEETING ABSTRACT)

Gaillard D, Behar C, Birembaut P, Ploton D, Daoud S, Morville P, Munzer M
Centre Hospitalier Universitaire, Reims, France
Excerpta Med Int Congr Ser; 570:295 1982

Cystic partially differentiated nephroblastoma is a Wilms' Tumor variant of infancy and early childhood that has been reported variously under many names. It is an uncommon lesion: 24 cases have been described in the literature. The purpose of this paper is to present another case and to point out a few original morphologic features. A 15 months old boy was hospitalized for an abdominal mass in the right flank. Intravenous pyelography revealed a distortion of the lower renal pelvis by a huge tumor. It appeared to have an heterogeneous echostructure with cystic and necrotic figures. Chemotherapy reduced the volume of the mass before nephrectomy. The excised kidney weighed 445 g. At the lower pole of the kidney a cystic, necrotic, pseudo-encapsulated mass of 9 cm in largest dimension, had the typical pathologic features of a cystic partially differentiated nephroblastoma with blastema, tubular structures and many striated muscle cells or rhabdomyoblasts in the mesenchyme. The cysts communicated neither with each other nor with the renal pelvis. This tumor appears to be made of very immature tissue: like the embryonic ducts, fibronectin is localized within the tubular basement membranes, and there is lot of type I collagen in the mesenchyme. But contrary to

embryonic kidney, there are no leucine amino peptidases in the tubular cells of the tumor. Those very immature features and the possible occurrence of numerous mitoses in the blastematic elements are arguments in favor of a malignant potential tumor and regular follow up is recommended. (no Refs)

32. SELECTIVE SURFACE STAINING OF BLADDER TUMORS BY INTRAVESICAL METHYLENE BLUE WITH ENHANCED ENDOSCOPIC IDENTIFICATION (MEETING ABSTRACT)

Gill WB, Huffman JL, Lyon ES, Schoenberg HW, Bagley DH, Straus FH
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Methylene blue has been extensively used in humans for localization of ureteral orifices, fistulae and for therapy of cystitis and urolithiasis. After observing that methylene blue only stained injured urothelium (chemical or mechanical damage) when instilled into rat bladders, we postulated that this dye might selectively bind to the surfaces of bladder tumors, but not to normal urothelium. Staining of human bladder tumors in vivo was accomplished by the intravesical instillation of 0.1% methylene blue in 0.9% saline through a foley catheter under 20 cm of hydrostatic pressure up to a maximum volume of 400 ml. After 5 minutes contact time, the methylene blue soluton was drained, and the bladder was washed twice with saline. Thereafter, either cystoscopy or operation was performed. Intravesical instillation of methylene blue resulted in selective surface staining of bladder tumors in vivo without staining the background of normal urothelium. This method has been employed in 22 patients with transitional cell carcinomas to date: 15 received endoscopic fulguration/resection and 7 underwent total cystectomy. The transitional cell carcinomas in 20 of these 22 patients bound methylene blue to the surfaces of the tumors usually bound the dye more extensively than lower grades. The two patients, whose tumors did not bind methylene blue, had received previous chemotherapy, which might account for their being falsely negative. Areas of hyperplasia and radiation cystitis also did not bind methylene blue. (no Refs)

33. HISTOPATHOLOGICAL ANALYSIS OF PRENEOPLASTIC CHANGES DURING N-BUTYL-N-(4-HYDROXYBUTYL)-NITROSAMINE-INDUCED URINARY BLADDER CARCINOGENESIS IN RATS.

Fukushima S, Murasaki G, Hirose M, Nakanishi K, Hasegawa R, Ito N
First Dept. Pathology, Nagoya City Univ. Medical Sch., 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 467, Japan
Acta Pathol Jpn; 32(2):243-250 1982

Sequential microscopic alterations of the urinary bladder epithelium during carcinogenesis were examined in rats after oral administration of 0.01% or 0.05% N-butyl-N-(4-hydroxybutyl)nitrosamine (BBN). Simple hyperplasia appeared after 4 wk of BBN administration. This regressed by 12 wk after BBN discontinuation but reappeared focally in some areas afer 20 wk and persisted to the termination of the experiment. Preneoplastic papillary or nodular hyperplasia appeared earlier and more frequently in rats treated with 0.05% BBN than in those treated with 0.01%, but these lesions regressed gradually during a prolonged observation period after BBN was discontinued. These results suggest that two types of papillary or nodular hyperplasias exist, one reversible and the other irreversible. Tumors appeared earlier in rats treated with 0.05% BBN than in those with 0.01% BBN. (Author abstract) (17 Refs)

34. ALTERATIONS AT THE EPITHELIAL-STROMAL INTERFACE IN CARCINOMA OF THE RAT BLADDER (MEETING ABSTRACT)

Memoli VA, Pauli BU
Department of Pathology, Rush, Presbyterian-St. Luke's Medical Center, Chicago, IL
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-3, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

Substantial alterations occur at the epithelial-stromal interface during the course of progression of a tumor from a noninvasive to an invasive state. These alterations at the epithelial-stromal junction in carcinogen (FANFT)-induced noninvasive carcinomas of rat urinary bladder were compared with control normals, using quantitative electron microscopy. Our results indicate an increased number of epithelial interdigitations within submucosal connective tissue in noninvasive and invasive carcinomas relative to controls. Perimeter length of the basal plasma membrane per unit length of submucosal tissue circumference (STC) shows a 56 per cent increase in invasive carcinoma, relative to controls. Although the perimeter of the basement membrane per STC is increased in early noninvasive carcinoma, it is decreased in invasive carcinoma, to 16 per cent of controls. These findings represent not only a marked increase in the contact area between tumor and submucosa, but an increase in the direct contact area between basal tumor cells and connective tissue stroma. This increase in direct contact area may contribute to the efficacy of matrix degradation by membrane-associated proteinases, which have been shown to be increased in invasive rat bladder tumors. The loss of basement membrane in invasive carcinomas is paralleled by a decrease in the number of hemidesmosomes per unit length of basal plasma membrane. Since hemidesmosomes anchor epithelial cells to their basement membrane, it is reasonable to suggest that focal reductions in hemidesmosome numbers, accompanied by decreased numbers of desmosomes, would reduce adhesion between tumor cells and the underlying connective tissue. (no Refs)

35. CYTOGENETIC ABERRATIONS IN BLADDER CARCINOMA (MEETING ABSTRACT)

Roy JB, Dagg C, Bottomley RH
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Predicting the natural history of an early bladder tumor in any given patient poses a vexing problem. This is due to the fact that 70% of initial tumors recur and approximately 20% of them will eventually become upgraded, invasive and/or metastasize. Presently the routine histopathologic evaluation of resected tumors is of little value in differentiating tumors of low biologic potential from those that will ultimately prove fatal. The specific objective of our work is to evaluate the role of chromosomal aberrations in vesical cancer as a means of prognosticating the malignant behavior of those tumors. Specimens from 30 patients with transitional cell carcinoma were obtained and separated into 2 parts. One part was sent for routine histological exam and the other for chromosomal analysis. Chromosomal preparations were obtained by mincing the tissue in a special medium. The cell suspension was incubated with Colcemid followed by cell wall lysis with hypotonic KCL. After

staining with Giemsa, metaphase spreads were counted and karyotypes were prepared. The histologic grade and stage of these 30 patients were correlated with their chromosomal analysis. The result showed that all 17 patients with low grade/stage had diploid or near diploid modal numbers with narrow distribution. On the other hand the 13 patients with high grade/stage tumors displayed aneuploidy with hyperdiploid modes and occasionally presence of marker chromosomes. (no Refs)

36. CHROMOSOMAL CONSTITUTION AND DNA DISTRIBUTION IN BLADDER CANCER (MEETING ABSTRACT)

Wijkstrom HE, Granberg-Ohman IF, Tribukait BF
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Chromosome analysis using in-vivo technique was performed in 108 tumors from 88 patients with transitional cell carcinoma. In 63 instances analyzable metaphases were obtained. The DNA distribution was measured with flow-cytometry in 71 tumors; in 51 tumors the two methods could be directly compared. In 27 noninvasive tumors of WHO grades 1 and 2 the modal populations were diploid-peridiploid in 23. Marker chromosomes were present only occasionally. The DNA content was 2c in 27 of 30 tumors analyzed by flow cytometry. Ten of 13 invasive grade 2 tumors had chromosomal modes in the diploid-peridiploid region. In the 3 initially aneuploid cases there was a subsequent histologic progression to grade 3, indicating a possible predicative value of this abnormality. Peridiploidy, markers and kariotype deviations appeared more often than in the noninvasive tumors. The DNA content was 2c in 9 tumors and 3.4-4.2 c in 5 (including the 3 mentioned above). The peridiploid deviation seen by chromosome analysis could not be detected by flow cytometry. In 23 grade 3 tumors aneuploidy (tri-and tetraploid modes) was seen in 17. There were no normal karyotypes. Several markers of various types were seen in the majority of the counted metaphases in all tumors. Twenty-five of 27 tumors had aneuploid DNA distributions by flow cytometry but the values were constantly 10-15% above the corresponding numerical chromosome count. Chromosomal analysis is not yet a method for clinical routine, except in selected patients, mainly because of banding problems. DNA analysis on the other hand may already be used as a complement to conventional grading. The numerical differences between the two methods has to be explained in order to exactly define the degree of ploidy. (2 Refs)

37. THE SIGNIFICANCE OF PLOIDY AND PROLIFERATION IN THE CLINICAL AND BIOLOGICAL EVALUATION OF BLADDER TUMORS: A STUDY OF 100 UNTREATED CASES.

Tribukait B, Gustafson H, Esposti PL
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Br J Urol; 54(2):130-135 1982

Cell material from 100 cases of newly diagnosed bladder tumors was studied with rapid flow cytofluorometric DNA analysis. The degree of ploidy and the percentage of cells in the S-phase characterizing the proliferation pattern of the tumors were determined from DNA histograms. The results were related to the tumor categories and to the histopathological grading of the tumors. Approximately 40% of T1 tumors showed aneuploid DNA patterns, while in the other categories aneuploidy was found in almost all cases. With few exceptions, tumors of Grade 1 were found to be diploid and tumors of Grade 3 aneuploid. In tumors of Grade 2, two-thirds were diploid and one-third aneuploid. In the group of aneuploid tumors the tetraploid cases exhibited the least malignant characteristics as judged by histological grades and tumor categories. The aneuploid non-tetraploid tumors increased in malignancy the more they deviated from tetraploidy. This might be explained by our observations of a positive correlation between the degree of ploidy and the degree of proliferation. The proliferation increased from 10% in tetraploid tumors to 20% in triploid and pentaploid tumors. (Author abstract) (14 Refs)

38. URINARY BLADDER CYTOLOGY AND IMMUNOPEROXIDASE STAINING FOR CARCINOEMBRYONIC ANTIGEN (MEETING ABSTRACT)

Bolleau MA
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The overall cytological accuracy for patients with histologically proven urothelial tumors is approximately 70% but varies significantly with the grade of the bladder tumor. In cases of moderately differentiated and poorly differentiated transitional cell tumors cytologies are positive in over 90% of cases. However well differentiated lesions yield negative cytology because the morphologic changes in the exfoliated cells are not sufficient to differentiate from normal cells. It has been reported that approximately 60% of well differentiated urothelial tumors have CEA (carcinoembryonic antigen)-containing cells. In an effort to increase the accuracy of cytology we have utilized immunoperoxidase staining for CEA in patients with low grade urothelial tumors. Bladder washings were obtained from 30 patients with known transitional cell carcinoma of the bladder and fixed with 50% ethanol. The cells were then placed in a cytospin centrifuge and spun on to microscope slides. An indirect immunoperoxidase labelled anti-CEA antibody technique was then used to identify urothelial cells containing CEA. A CEA-producing colon carcinoma cell line was used as a positive control. Slides from 5 patients were considered uninterpretable. Slides from 15 patients revealed urothelial cells containing CEA. Slides from the remaining 10 patients were negative. (no Refs)

39. HISTOCHEMISTRY OF NADH DIAPHORASE AND GAMMA-GLUTAMYLTRANSPEPTIDASE IN RAT BLADDER TUMORS.

Vanderlaan M, Fong S, King EB
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Carcinogenesis; 3(4):396-402 1982

To improve identification of preneoplastic bladder cancer cells, we have studied two enzyme histochemical changes in bladder tumors induced in male Fisher 344 rats by the carcinogen N-butyl-N-(4-hydroxybutyl)-nitrosamine. In early areas of focal nodular hyperplasia there was a dramatic increase in staining for NADH:menadione oxidoreductase (diaphorase) activity. In nonfocal areas as well, there were many individual cells with intense staining, while the controls were of uniform moderate staining. Large papillomas and carcinomas often showed heterogeneous staining. Gamma-glutamyltranspeptidase (GGT) was absent from normal urothelium and from all

rs except the most advanced carcinomas and large papillo- In old, carcinogen-exposed animals, GGT activity was in the luminal surface of tumors and in the interlesion elium. In newborn rats and in rats with regenerative hy- lasia following wounding of the urothelium, the diaphor- taining was less than that in the untreated adult. Our find- suggest that increased diaphorase activity may serve to ify early islands of carcinogen-induced, enzymatically al- l bladder cells, while GGT will not. (Author abstract) (23)

NVASIVENESS IN VITRO USED AS A CRITERION MALIGNANCY OF HUMAN BLADDER EPITHELIAL LS PROPAGATED IN CULTURES (MEETING TRACT)

ristensen B, Don P, Vilien M, Kieler J
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Meeting of the European Association for Cancer Research, Octo- ber 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

oping to establish cultures of human bladder epithelium as odel for studies of chemical carcinogenesis in vitro we have e a comparative study of normal 'spontaneously' trans- ned, and tumor-derived urothelial cells propagated in vitro. nor production on sc inoculation into nude mice, and inva- and destructive growth in mixed cultures of fragments of ryonic chick hearts associated with aggregates of tumor s served as criteria of malignancy. The morphological char- eristics, growth pattern, and nutritional requirements of in- ing and non-invading cells will be described. (no Refs)

DIETHYLSTILBESTEROL INDEPENDENT GROWTH ESTROGEN INDUCED/DEPENDENT RENAL ENOCARCINOMA CELLS IN CULTURE (MEETING STRACT)

aylor PH, Loring JM, Villee CA
epartment of Biological Chemistry, Harvard Medical School, Boston, MA

48th National Meeting of the American Association for the Advance- ment of Science, January 3-8, 1982, Washington, D.C. American As- sociation for the Advancement of Science 182 pp., 1982.

Understanding the mechanism of hormone induced and/or pendent tumor growth is critical to both prevention and con- l of many neoplasms. Both estradiol and diethylstilbesterol ES) at pharmacological concentrations in serum induce al adenocarcinoma in the Syrian hamster. Since primary nors require DES for growth when transplanted, we have en studying renal carcinomas in primary culture to define the uirements for tumor growth. Cell growth is assessed both the numbers of cells 6 days' post culture and by DNA syn- etic activity as measured by radiolabeled thymidine incorpo- ion at days 3 and 6 post culture. Fetal calf serum (10%) ded to minimal essential media increases cell growth and NA synthesis compared to 10% calf serum supplemented edia. DES does not constantly increase either cell growth or NA synthesis under any conditions tested. These results are erpreted as being consistent with our developing hypothesis at DES is acting indirectly (most probably via a pituitary oduct) rather than directly affecting tumor cell growth. (no efs)

42. IN VITRO CARCINOGENESIS IN CANINE BLADDER (MEETING ABSTRACT)

Klaunig JE, Constantini MG, Barut BA, Goldblatt PJ
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71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massa- chusetts. International Academy of Pathology 95 pp., 1982.

As part of our overall investigation of mechanisms of blad- der carcinogenesis, we have developed methods for establish- ing primary and secondary cultures of canine bladder urothe- lial cells. Urinary bladders from adult dogs of mixed breed were removed immediately after exsanguination. Four pieces of bladder (0.5 x 0.5 cm) were placed urothelium side up per 60-mm culture dish. Two milliliters of Ham's 151 culture medium were added per dish, and dishes were maintained at 36.5 C in a humidified CO2 incubator. Epithelial cells were seen extending from the explants 2 to 3 days after culture initi- ation. Within 2 to 3 weeks cells were almost confluent on the culture dish. The inclusion of fetal bovine serum in the medium resulted in the overgrowth of epithelial cultures by fibroblasts. The calcium concentration in the medium had a significant in- fluence on differentiation and growth of primary urothelial cells. A concentration of 1 x 10(-4) M calcium appeared opti- mal for cell growth and prevention of differentiation. Second- ary cultures were initiated by trypsinization of primary cul- tures. Fetal bovine serum was required in the medium for sec- ondary culture cell growth. DNA repair (measured by induc- tion of unscheduled DNA synthesis (UDS)) was evident in ex- plants, primary, and secondary cultures following exposure to methylnitrosourea, aflatoxin B1, 4-aminobiphenyl, and benzo(a)pyrene. UDS in each compound displayed a linear dose response. Radiolabeled benzo(a)pyrene was metabolized and covalently bound to DNA in bladder explants primary and secondary cultures. (no Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

43. COMPARISON BETWEEN THE METHODS OF INDIRECT IMMUNOFLUORESCENCE AND SPECIFIC RED CELL ADHERENCE IN DETECTING ABH ISO-ANTIGENS IN BLADDER CARCINOMA.

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Am J Clin Pathol; 77(5):548-554 1982

We compared the method of indirect immunofluorescence (IIF) with that of specific red blood cell adherence (SRCA) for detecting ABH blood group substance (BGS) on Stage O papillary transitional cell carcinoma (TCC) of the bladder. In evaluating BGS 'positivity' or 'negativity' both methods gave identical results. The IIF is somewhat easier to perform and less subjective in interpretation while the SRCA method needs only a conventional light microscope and the slides themselves are permanent 'records'. In cases of questionable reactivity with the SRCA, the IIF was a helpful adjunct. The IIF method is a viable option to the SRCA method when studying TCC for BGS. (Author abstract) (14 Refs)

44. COMBINATION OF ABH AND T ANTIGEN DETECTION IN PROGNOSIS OF URINARY BLADDER CARCINOMA (MEETING ABSTRACT)

Coon JS, Weinstein RS, Summers JL
Department of Pathology, Rush-Presbyterian-St. Luke's Medical Center, Chicago, IL
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

Expression of the ABH blood group antigens (BGAg) by human bladder cancer implies a good prognosis, but BGAg-negative tumors are unpredictable. The T antigen (Thomsen-Friedenreich antigen:TAg), a precursor of other BGAg, has previously been found in malignant, but not most normal, cells in which the TAg is cryptic but can be unmasked with neuraminidase (NMD). We investigated the prognostic significance of TAg expression in bladder cancer by staining paraffin sections with a T-specific lectin (peanut agglutinin (PNA) immunoperoxidase technique. Seventy-two cases of low grade, low stage bladder cancer, 21 cases of high grade bladder cancer, and 68 controls were studied. All normals expressed the TAg only after NMD treatment (cryptic TAg+). The grade III cancers, all invasive, either expressed the TAg (TAg+) (67 per cent) or lacked T even after NMD (cryptic TAg-) (29 per cent), indicating that the T structure was lost rather than masked as in normal tissue. Thirty-nine per cent of 23 grade I and II cancers that were TAg+ or Cryptic TAg- subsequently became invasive (less than stage A), compared with 10 per cent of 49 cryptic TAg+ cancers. For 32 grade I and II, ABH BGAg-negative cancers, 64 per cent of TAg+ or cryptic TAG- cancers became invasive compared with 17 per cent of cancers that had cryptic TAg+. Thus, the combination of both marker systems was better than either system used alone to identify bladder cancers with a high aggressive potential. (no Refs)

45. ALTERATIONS IN SPECIFIC CARBOHYDRATE RESIDUES IN NEOPLASTIC TRANSITIONAL EPITHELIUM (IE, UROTHELIUM) OF HUMAN URINARY BLADDER (MEETING ABSTRACT)

Alroy J, Gavris V, Heaney J, Szoka F, Ucci A
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71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1981.

The antigenic nature of bladder urothelium is determined by carbohydrate residues of the cell surface coat. Loss of three specific carbohydrate residues (ie, ABH isoantigens) in neoplastic urothelium (red cell adherence test) is associated with tumor invasion and is a predictor of the clinical course. However, little is known about other surface carbohydrates of neoplastic and non-neoplastic urothelium. In this study, fluorescein isothiocyanate (FITC)-conjugated lectins were used to detect specific carbohydrate residues in neoplastic urothelium of 16 patients and compared with urothelium of 16 patients with non-neoplastic urologic disorders. Paraformaldehyde-fixed specimens were incubated with the following lectins: Ricinus communis-1 (RCA-1), Ulex europeus-1 (UEA-1), Archis hypogaea (PNA), Glycine max (SBA), Canavalia ensiformis (Con-A), Triticum vulgare (WGA), Dolichos biflorus (DBA), and Limulus polyphemus (LPA). Additional tissues were treated with neuraminidase to cleave sialic acid residues prior to incubation with PNA. Incubaton with blocking carbohydrates served as a specific negative control. RCA-1, Con-A, WGA, and LPA bound to neoplastic and non-neoplastic urothelium in all specimens. However, binding intensity varied among different neoplasms. After treatment with neuraminidase, PNA bound to all specimens except two neoplasms. UEA-1 bound to non-neoplastic urothelium in eight patients with type H blood and to some neoplastic cells in patients with type A blood. DBA bound only to non-neoplastic urothelium in eight patients with type A blood. SBA bound to blood vessel endothelium in all specimens and to metaplastic urothelium in only two patients. (no Refs)

46. HUMAN BLADDER TUMOR ASSOCIATED SURFACE ANTIGENS (MEETING ABSTRACT)

Sramek SJ, Reichert DF, Smith KO, Lamm DL
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

A rabbit antiserum was prepared against the human transitional cell carcinoma cell line T24 to characterize possible tumor associated surface antigens. T24 antiserum demonstrated significant reactivity with human bladder tumor antigens and normal bladder antigens by radioimmunoassay (RIA). After repetitive absorption with a pool of antigens collected from normal urine sediments no reactivity with normal bladder antigens could be detected by RIA. The absorbed rabbit antiserum was tested with T24 labeled by one of two methods. Lactoperoxidase-catalyzed radioiodination of intact cells was used to label surface proteins and metabolic labeling with C14 glucosamine was used to label glycoproteins. The immune complexes were isolated on sepharose-bound staphylococcal protein A and then analyzed by SDS (sodium dodecyl sulfate) polyacrylamide gel electrophoresis. The majority of the I-125 radioactivity isolated by the immune serum was distributed in seven peaks with the following molecular weights: 1) 170K; 2) 130K; 3) 120K; 4) 70K; 5) 45K; 6) 42K; 7) less than 30 K. In metabolically-labeled cells, glucosamine radioactivity coincided with peaks 3, 6, and 7. The T24 extract released two proteins from patient immune complexes with a mobility in SDS gel identical to peaks 3 and 5. The rabbit anti-T24 serum appears to identify a family of surface and glycosylated tumor-associated antigens. Two of these antigens may be similar to circulating antigens in immune complexes from patients with transitional cell carcinoma. (no Refs)

47. ANTIBODY INDUCED IN MICE USING A HUMAN TRANSITIONAL BLADDER CARCINOMA CELL LINE (MEETING ABSTRACT)

Fessia SL, Jensen MD, Bruce AS
University of Lowell, Lowell, MA, 01854
Fed Proc; 41(3):938 1982

A human tumor line (RT-4) was used to induce antibodies in 5-wk old BALB/cj mice. Mice were immunized IP with 10(6) cells/mouse followed 3 wks later then 2 wks later by 5x106cells/mouse. Serum samples taken 2 wks after third injection were tested using indirect immunofluorescence (IIF) and radioimmunoassay (RIA). RIA showed 58.9 ng/10(5) cells (n equals 8) of mouse immunoglobulin bound to RT-4 cells and 58.1 ng/10(5) cells (n equals 4) bound to cells from a bladder tumor biopsy. Normal exfoliated bladder epithelial cells (NXF) bound 38.6 ng/10(5) cells (n equals 7). Binding to a non-related human cell line, adeno-carcinoma of the colon (HT-29) was 51.9 ng/10(5) cells (n equals 4). T-tests showed a significant difference in the binding to RT-4 and bladder tumor cells compared to binding to NXF. Maximum binding was retained in 1/10 dilution of serum samples. There was no significant differ-

ence between binding to NXF and HT-29. IIF showed high density fluorescence to RT-4 and tumor cells while HT-26 and NXF showed low density fluorescence. These data indicate the feasibility of this technique for our studies now in progress for the development of monoclonal antibodies to bladder cancer cells. (no Refs)

48. IDENTIFICATION OF AN ANTIGEN ASSOCIATED WITH TRANSFORMING GENES OF HUMAN AND MOUSE MAMMARY CARCINOMAS.

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Proc Natl Acad Sci USA; 79(10,part1):3315-3319 1982

Sera from tumor-bearing mice immunoprecipitated an 86,000-dalton glycoprotein from extracts of NIH cells transformed by human mammary carcinoma DNA. This antigen was not immunoprecipitated from extracts of NIH 3T3 cells, spontaneously transformed NIH cells, NIH cells transformed by normal human DNA, NIH cells transformed by human bladder carcinoma DNA, or NIH cells transformed by Rous sarcoma virus DNA. In addition, sera from mice bearing tumors induced by NIH cells transformed by either normal human DNA or human bladder carcinoma DNA did not immunoprecipitate this antigen from extracts of NIH cells transformed by human mammary carcinoma DNA. However, this antigen was immunoprecipitated by sera from mice bearing tumors induced by NIH cells transformed by mouse mammary carcinoma DNAs and from mice bearing primary mammary carcinomas. These results indicate that this glycoprotein represents an antigen that is specifically associated with expression of the transmissible transforming genes of human and mouse mammary carcinomas. (Author abstract) (15 Refs)

REVIEWS AND OTHER RELATED STUDIES

49. RETINOIDS, URINARY BLADDER CARCINOGENESIS, AND CHEMOPREVENTION: A REVIEW AND SYNTHESIS.

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Nutr Cancer; 3(2):109-115 1981

An analysis of the effects of natural (vitamin A) and synthetic retinoids on experimental carcinogenesis of the urinary bladder indicates that inhibitory activity is carcinogen- or carcinogen-class-specific. These findings suggest that there may be more than one pathway for the neo-differentiation of urothelial cells to frank carcinoma and that these pathways may be related to both carcinogen class and dietary vitamin A status. (Author abstract) (54 Refs)

50. HORMONES AS ETIOLOGICAL AGENTS IN NEOPLASIA.

Furth J
Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

Hormones as etiological agents in neoplasia are discussed. The basic properties of human hormones are reviewed, and general considerations in the detection of hormonal activity are listed. Brief general comments are presented on tumors in peripheral areas illustrating the diversity of pathogenic mechanisms by which hormones can produce tumors. Peripheral tumors are of two kinds: those affecting non-hormone-secreting organs, which do not feed back (as with the mammary gland), and those affecting peripheral hormone-secreting organs, which do. The best example of the former is the mammary tumor, and good examples of the second type are thyroid and ovarian tumors. Other tumors which are hormonally related include adrenal tumors which are unique in that they can give rise to four or more types of tumors - estrogen, androgen, glucocorticoid, and mineralocorticoid secreting - and in that they have different types of inductive mechanisms. Renal cortical carcinomas are induced by estrogens in male hamsters. Human placental lactogen stimulates carcinogenesis in young rats. It promotes mammary tumorigenesis during pregnancy, both directly and indirectly, through its promotion of progesterone secretion by the ovary. Thyrocalcitonin is the hypocalcemic polypeptide hormone secreted by the medullary cells of the thyroid. These cells can give rise to medullary thyroid carcinoma. (286 Refs)

51. ONCOGENES IN HUMAN TUMOR CELL LINES: MOLECULAR CLONING OF A TRANSFORMING GENE FROM HUMAN BLADDER CARCINOMA CELLS.

Pulciani S, Santos E, Lauver AV, Long LK, Robbins KC, Barbacid M
Lab. Cellular and Molecular Biology, NCI, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 79(9):2845-2849 1982

The presence of dominant transforming genes in human tumor cell lines has been investigated. High mol wt DNAs isolated from cell lines established from carcinomas and sarcomas of various organs as well as from a glioblastoma and two melanomas were utilized to transfect NIH/3T3 mouse fibroblasts. The DNAs of T24 and A2182, two cell lines derived from a bladder and a lung carcinoma, respectively, and of HT-1080, a cell line established from a fibrosarcoma, were able to transform recipient NIH/3T3 cells. First-cycle transformants exhibited anchorage-independent growth and were tumorigenic in athymic and immunocompetent mice. Moreover, they contained human DNA sequences and were able to transmit their malignant phenotype in additional cycles of transfection. Southern blot analysis of T24-derived transformants showed that a single fragment of human DNA specifically cosegregated with the malignant phenotype, suggesting that it contained the T24 oncogene. Therefore, these human sequences were molecularly cloned with lambda Charon 9A as the cloning vector. The resulting recombinant DNA molecule, designated lambdaT24-15A, was shown to contain a 15-kilobase-pair EcoRI insert of human cellular DNA. LambdaT24-15A DNA (either intact or EcoRI digested) transformed NIH/3T3 fibroblasts with a specific activity of 20,000 focus-forming units per pmol of cloned DNA. Our results indicate that we have molecularly cloned a biologically active oncogene present in T24 human bladder carcinoma cells. (Author abstract) (28 Refs)

52. TRANSFORMING GENES OF A HUMAN BLADDER CARCINOMA (MEETING ABSTRACT)

Shih C, Weinberg RA
Center for Cancer Research and Department of Biology, Massachusetts Institute of Technology, Cambridge, MA
Thirty-fifth Annual Symposium on Fundamental Cancer Research, March 2-5, 1982, Houston, Texas. The University of Texas M. D. Anderson Hospital and Tumor Institute 38 pp., 1982.

We have undertaken a series of experiments to isolate genes whose alteration leads to induction of the transformed state within the cell. One example of this is the transforming gene present in DNA of the human bladder carcinoma cell line EJ. This gene was originally detected using calcium phosphate-mediated gene transfer (transfection). DNA of EJ bladder carcinoma cells is able to induce foci when applied to monolayer cultures of NIH3T3 mouse fibroblasts, indicating the presence of a discrete and potent transforming factor in the DNA of the tumor cells. Hybridization probes specific for these repeated sequences are able to detect the DNA carrying the human transforming gene amid a great excess of mouse DNA sequences. The DNA of a transfected mouse cell can be introduced into a bacteriophage vector and the resulting library screened for components specific for human DNA. In this manner we have isolated a chimeric bacteriophage whose DNA carries the transforming gene of the human EJ bladder carcinoma. This DNA exhibits strong focus-forming ability (greater than 10(4) focus-forming units per microgram). Its use as sequence probe in Southern hybridizations reveals that the transforming gene is similar in structure to a sequence present in the DNA of a normal untransformed cell and, therefore, that this transforming gene arises by minor alteration of a sequence present in the normal cell's DNA. Use of this probe also demonstrates relatedness with transforming gene of the independently derived T24 bladder carcinoma line. (no Refs)

53. ENHANCED GROWTH OF HUMAN RENAL CELL CANCER IN CONDITIONED NUDE MICE (MEETING ABSTRACT)

Williams RD, Dombrovskis S
No affiliation given
77th Annual Meeting of the American Urological Association, Inc; May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

The athymic nude mouse because of its congenital immune deficiency is a congenial host for human tumor production and has been used widely as a model for study of human tumor biology. Unfortunately, not all human tumors grow in these animals and rarely do they metastasize. In an attempt to develop a model for growth of primary human renal cell carcinoma (RCC) grafts with the possibility of metastases we studied the hypothesis that pretreating newborn nude mice with human RCC ghosts SC, followed by a challenge of viable RCC cells SC at six weeks would enhance tumor formation. Three cell lines of human RCC were inoculated into a total of 38 animals. Control animals were treated with media only at birth and viable cells SC at six weeks. Two human RCC cell lines did not produce tumors in either the experimental or control animals. Cell line 786-0 produced tumors in 95% of both control and experimental animals, however the tumors in experimental mice occurred earlier and grew more rapidly than in controls. Of particular importance the tumors in male experimental animals grew three times as fast as in female mice. No metastases were observed in any of these mice. We conclude that newborn male nude mice can be preconditioned with nonviable cells to enhance tumor formation from SC cells inoculated at six weeks, however because only 1 of 3 tumors grew, the procedure is not sufficient to produce a model for study of primary RCC grafts and metastases. (no Refs)

54. TUMOR IMPLANTATION IN THE BLADDER AFTER NONDENUDING INJURY (MEETING ABSTRACT)

Jones KW, Gill WB, Bagley DH
No affiliation given
77th Annual Meeting of the American Urological Association, Inc May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Intraluminal fulguration of the bladder produces a deep injury, denuding the mucosal surface and injuring muscle. N-methyl-N-nitrosourea (MNU), denudes the mucosal surface and causes submucosal edema. Both of these injuries have been shown to increase the rate of tumor implantation significantly over control (saline irrigated) bladders. In contrast intravesical instillation of either 5% Triton X100 or 0.1 NHCl produced a nondenuding bladder injury in which the epithelium was histologically intact. These chemical injuries allowed in vivo crystal adhesion or staining with intravesical dyes, which did not occur in the normal bladder. The rate of tumor implantation after injury with nondenuding agents is compared with that after injury with a denuding agent and with saline irrigated controls. The bladders of C3H/He mice were fulgurated or irrigated with either 0.1 N hydrochloric acid or 5% Triton X100. Fulguration was performed with 4-0 surgical wire insulated with a PE10 catheter placed transurethrally and attached to an electrocautery. Acid or Triton X100 was placed in the bladder through urethral catheters, left in place for two minutes and then washed out with saline. Control animals were catheterized and irrigated with saline. A single cell suspension of FANFT(N[4-(5-nitro-2-furyl)-2 thiazolyl]formamide) induced tumor cells was placed in the bladder. The rate of tumor implantation was 70% in the fulgurated group and 20% in the control group. The implantation rates following 0.1N hydrochloric acid (0%) on 5% Triton X100 (8%) were not significantly different from the controls. Bladder injuries with these nondenuding injuring agents did not increase the tumor implantation rate significantly beyond that of controls, whereas the denuding injury of fulguration increased tumor implantation. (no Refs)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. MICROWAVE HEATING ENHANCES THE MIGRATION OF PLASTICIZERS OUT OF PLASTICS.
Bishop CS, Dye A
East Tennessee State Univ., Johnson City, TN, 37614
J Environ Health; 44(5):231-235 1982

2. DISEASES CAUSED BY EPOXY RESINS.
Konietzko H, Fischer G
Institut fur Arbeits- und Sozialmedizin, Johannes-Gutenberg-Universitat, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
Zentralbl Arbeitsmed Arbeitsschutz Proph; 32(3):86-91 1982
In GER

3. NITROSAMINES.
Aigner K
Pneumonologische Abteilung, Krankenhaus der Elisabethinen, Fadingerstr. 1, A-4020 Linz-Donau, Austria
Wien Med Wochenschr; 132(71,Suppl):75-79 1982
In GER

4. EXPERIMENTAL TUMORS OF THE PERIPHERAL NERVOUS SYSTEM.
Beniashvili DS
Cancer Res. Center, Tbilisi, USSR
Eksp Onkol; 4(2):12-19 1982
In RUS

5. MUTAGENIC, CARCINOGENIC AND TERATOGENIC EFFECTS OF STYRENE.
Sram RJ, Pohlova H, Topinkova E
Klinika hygieny a epidemiologie, Srobarova 48, 100 42 Prague 10, Czechoslovakia
Prac Lek; 34(2):68-72 1982
In CZE

6. DIETHYLSTILBESTROL: EFFECT OF IN UTERO EXPOSURE.
Burke L
Obstetrics/Gynecology Dept., Harvard Medical Sch., Boston, MA
Curr Probl Obstet Gynecol; 5(2):1-58 1981

7. IN UTERO EXPOSURE TO DIETHYLSTILBESTROL: ADVERSE EFFECTS ON THE REPRODUCTIVE TRACT AND REPRODUCTIVE PERFORMANCE IN MALE AND FEMALE OFFSPRING.
Stillman RJ
Dept. Obstetrics and Gynecology, George Washington Univ. Sch. Medicine and Health Sciences, 2150 Pennsylvania Ave., NW, Washington, DC, 20037
Am J Obstet Gynecol; 142(7):905-921 1982

8. BIOLOGICAL EFFECTS OF MINERAL WOOL.
Petersen R, Ehrhorn H, Mousing K, Sabroe S, Silberschmid M, Venstrup-Nielsen SE
Socialmedicinsk institut, Vesterbro Torv 1-3, DK-8000 Arhus C, Denmark
Ugeskr Laeger; 144(13):971-975 1982
In DAN

DIETARY FACTORS IN CARCINOGENESIS

9. NATURALLY OCCURRING FOOD TOXICANTS: PHENOLIC SUBSTANCES OF PLANT ORIGIN COMMON IN FOODS.
Singleton VL
Dept. Viticulture and Enology, Univ. California, Davis, CA
Adv Food Res; 27:149-242 1981

10. MUTAGENS, CARCINOGENS, AND TUMOR PROMOTERS IN OUR DAILY FOOD.
Sugimura T
Natl. Cancer Res. Inst., Tsukiji, Chuo-ku, Tokyo, Japan
Cancer; 49(10):1970-1984 1982

11. THE BIOLOGICAL EFFECTS OF CARRAGEENAN AND OTHER SULFATED POLYSACCHARIDES WITH PARTICULAR ATTENTION TO IMMUNOLOGICAL AND CARCINOGENIC PROPERTIES.
Larsen B
Kraeftforskningsinstituttet, DK-8000 Arhus C, Denmark
Ugeskr Laeger; 144(12):860-863 1982
In DAN

12. VARIATIONS AMONG SPECIES AND CELL TYPES IN THE EFFECTS OF CAFFEINE ON MUTAGEN-INDUCED CYTOTOXICITY AND POSTREPLICATION REPAIR OF DNA.
Sivak A, Rudenko L, Teague LG
Arthur D. Little, Inc., Cambridge, MA, 02140
Environ Mutagen; 4(2):143-162 1982

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

13. CANCER IN THAILAND: LESSONS FOR CANCER CONTROL.
Miller DG, Somboonchareon S
Strang Clinic, Preventive Medicine Inst., 55 East 34th St., New York, NY, 10016
Prev Med; 11(2):232-239 1982

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Greenberg ER, Colton T, Bagne C
Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center, Hanover, NH, 03755
JNCI; 68(5):743-750 1982

15. STUDIES OF CANCER EPIDEMIOLOGY IN THE UNITED STATES OF AMERICA.
Lapin IuE
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Feldsher Akush; (2):55-57 1982
In RUS

16. CURRENT CONCEPTS OF THE ETIOLOGY AND PATHOGENESIS OF LUNG CANCER.
Chaklin AV, Gritsiute LA
No affiliation given
Vopr Onkol; 28(2):3-9 1982
In RUS

17. ETIOLOGY OF MOUTH AND LIP TUMORS.
Zabezhinskii MA, Godorozha PD
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Vopr Onkol; 28(2):105-113 1982
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Peterson LG, Popkin MK, Hall RC
P.O. Box 20708, 6431 Fannin, Houston, TX, 77025
Psychosomatics; 22(9):774-793 1981

19. PREDICTIVE IDENTIFICATION OF HYPERSUSCEPTIBLE INDIVIDUALS.
Omenn GS
Dept. Environmental Health, Univ. Washington, Seattle, WA, 98195
JOM; 24(5):369-374 1982

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Neiman IM
No affiliation given
Patol Fiziol Eksp Ter; (2):63-70 1981
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21. POLYCHLORINATED BIPHENYLS (PCBS): AN AUSTRALIAN VIEWPOINT ON A GLOBAL PROBLEM.
Richardson BJ, Waid JS
Marine Science Lab., Ministry for Conservation - Victoria, P.O. Box 114, Queenscliff, Victoria 3225, Australia
Search; 13(1/2):17-25 1982

22. SIGNIFICANCE OF ENVIRONMENTAL FACTORS FOR THE DEVELOPMENT OF LEUKEMIA, MYELOMA AND MALIGNANT LYMPHOMA.
Brandt L
Onkologiska kliniken, Lasarettet, Lund, Sweden
Lakartidningen; 79(15):1490-1492 1982
In SWE

23. ENVIRONMENTAL FACTORS AND MALIGNANT HEMATOLOGICAL DISEASES.
Bjorkholm M
Hematologsektionen, Danderyds sjukhus, Danderyd, Sweden
Lakartidningen; 79(15):1457-1459 1982
In SWE

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

24. REGULATION OF GENE EXPRESSION IN NORMAL AND NEOPLASTIC CELLS. A REVIEW.
Hochhauser SJ, Stein GS, Stein JL
Dept. Biochemistry and Molecular Biology, Univ. Florida, Coll. Medicine, Gainsville, FL, 32610
Pathobiol Annu; 11:1-29 1981

25. WHAT ARE ISOZYMES TELLING US ABOUT GENE REGULATION IN CANCER?
Weinhouse S
Fels Res. Inst., Temple Univ. Sch. Medicine, Health Sciences Center, Philadelphia, PA, 19140
JNCI; 68(3):343-349 1982

26. CHANGES IN AMINO ACID AND SUGAR TRANSPORT ACTIVITY ASSOCIATED WITH MALIGNANT TRANSFORMATION.
Nishino H, Inui K
Dept. Biochemistry, Kyoto Prefectural Medical Univ., Kyoto, Japan
Tanpakushitsu Kakusan Koso; 26(7):881-895 1981
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27. CURRENT VIEWS ON THE NATURE OF MYOEPITHELIAL CELLS AND THEIR ROLE IN THE MORPHOGENESIS OF DYSHORMONAL HYPERPLASIAS AND BREAST TUMORS.
Karelina TV
Central Lab. Pathology, Inst. Human Morphology, Moscow, USSR
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MODIFICATION OF CARCINOGENESIS

28. OVERVIEW: RETINOIDS AND CARCINOGENESIS.
Schramm T, Coutelle R
Zentralinstitut fur Krebsforschung, Akademie der Wissenschaften der DDR, Lindenberger Weg 80, DDR-1115 Berlin-Buch, E. Germany
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29. RETINOIDS, URINARY BLADDER CARCINOGENESIS, AND CHEMOPREVENTION: A REVIEW AND SYNTHESIS.
Lower GM, Kanarek MS
Dept. Veterinary Science, Coll. Agricultural and Life Sciences, Univ. Wisconsin, 1655 Linden Drive, Madison, WI, 53706
Nutr Cancer; 3(2):109-115 1981

30. THE ANTITUMOR POLYSACCHARIDE LENTINAN: AN OVERVIEW.
Chihara G
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Excerpta Med Int Congr Ser; 576:1-16 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

31. ENDOGENOUS ONCOGENIC TYPE B VIRUSES IN MICE.
Komarova EA, Kriukova IN
All-Union Cancer Res. Center, Moscow, USSR
Eksp Onkol; 4(2):3-12 1982
In RUS

32. GENETIC INTERACTIONS BETWEEN TUMOR VIRUSES AND HOST CELLS.
Rowe WP
Lab. Viral Diseases, Natl. Inst. Allergy and Infectious Diseases, NIH, Bethesda, MD, 20205
Cancer; 49(10):1958-1962 1982

33. THE PERSISTENCE OF RETROVIRUSES.
Weiss RA
Chester Beatty Res. Inst., Fulham Road, London SW3 6JB, England
Symp Soc Gen Microbiol; 33:267-289 1982

34. HOW DO PAPOVA VIRUSES PERSIST IN THEIR HOSTS?
Griffin BE
Imperial Cancer Res. Fund, Lincoln's Inn Fields, London WC2A 3PX, England
Symp Soc Gen Microbiol; 33:227-247 1982

35. THE EPSTEIN-BARR VIRUS: HISTORICAL, BIOLOGIC, PATHOLOGIC AND ONCOLOGIC CONSIDERATIONS.
Seemayer TA, Oligny LL, Gartner JG
Dept. Pathology, Montreal Children's Hosp., Montreal, Quebec, Canada
Perspect Pediatr Pathol; 6:1-33 1981

36. KAPOSI'S SARCOMA: WHY A 'HOMOSEXUAL DISEASE'?
Groopman JE, Gottlieb MS
Div. Hematology-Oncology, Univ. California at Los Angeles Sch. Medicine, Los Angeles, CA
Hosp Pract; 17(5):64F-64G,64J,64N,64O,64R,64T 1982

METHODOLOGY IN CARCINOGENESIS RESEARCH

37. MAJOR APPROACHES TO THE EXPERIMENTAL STUDY OF LUNG CANCER.
Plisa GB, Turusov VS, Zabezhinskii MA
No affiliation given
Vopr Onkol; 28(2):18-22 1982
In RUS

38. ON THE NECESSITY OF MUTAGENICITY TESTING OF NEW DRUGS.
Bogajewski J, Schoneich J
Zaklad Genetyki Czlowieka, PAN, 60-479 Poznan, Poland
Pol Tyg Lek; 37(2):63-67 198.
In POL

OTHER REVIEWS IN CARCINOGENESIS

39. CANCER - PRINCIPLES AND PRACTICE OF ONCOLOGY.
DeVita VT, Hellman S, Rosenberg SA

NCI, Bethesda, MD
Cancer - Principles and Practice of Oncology. Philadelphia, Lippincott, 1926 pp., 1982.

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Watson JD
Cold Spring Harbor Lab., Box 100, Cold Spring Harbor, NY, 11724
Cold Spring Harbor Symp Quant Biol 45(part 1): 445 pp., 1981.

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- **ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS..... 3-8**
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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. CANCER MORTALITY EXCESS.

Neuberger JS, Hollowell JG
Dept. Community Health, Univ. Kansas Sch. Medicine, Kansas City, KS
J Kans Med Soc; 83(5):244-248 1982

Cancer mortality by site and county in Kansas for the period 1973-1977 is reported. Data were restricted to white male and female residents of Kansas. Counties with elevated rates for 1950-1969 were compared with results for 1973-1977 to see if they remained consistently high for the same type of cancers. The only consistently high statistically significant mortality rates found in Kansas during both time periods were for lung cancer in white males in Cherokee and Wyandotte counties. Lung cancer mortality rates rose more rapidly than expected in females in Cherokee County to the point where lung cancer is presently comparable to breast cancer as the leading cause of female cancer mortality. Cancer sites which have increased in 1973-1977 to become statistically significantly elevated are male kidney cancer in Butler county, male bladder cancer in

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Shawnee county, and pancreatic cancer in Atchison county, (previously were not included). No significant excesses were found for females. Instability in rates due to small sample size were recognized as possible reasons for some of the calculated cancer mortality excess observed. (7 Refs)

2. INVERTED PAPILLOMA OF THE URINARY TRACT.

Anderstrom C, Johansson S, Pettersson S
Dept. Urology, Sahlgrenska sjukhuset, Univ. Goteborg, Goteborg, Sweden
J Urol; 127(6):1132-1134 1982

We report nine clinicopathological cases of inverted papilloma. The occurrence of associated true malignant epithelial tumors in the urinary tract in four patients is not concurrent with previous reports. Even though inverted papilloma per se is a benign lesion it may be associated with malignant epithelial tumors of the urinary tract. The similarity between proliferative lesions of the bladder and inverted papilloma is discussed. The possibility of common etiologic factors of proliferative cystitis, cystitis cystica, cystitis glandularis, inverted papilloma and ordinary bladder tumors may be considered. (Author abstract) (21 Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

3. INTRAUTERINE EXPOSURE TO SACCHARIN AND RISK OF CANCER OF THE URINARY BLADDER IN HUMANS.

Kamby C
Cancerregisteret, Strandboulevarden 49, DK-2100 Copenhagen 0, Denmark
Ugeskr Laeger; 144(20):1480-1482 1982

The incidence of cancer of the urinary bladder was studied on the birth cohort 1941-1945 compared with the birth cohorts 1931-1935 and 1936-1940 (all in the age bracket 20-34 yr) in view of the evidence of increased risk of bladder cancer due to intrauterine exposure to saccharin in experimental animals and to the increased consumption of saccharin during the period 1941-1945. The birth cohort 1941-1945 included 996,866 men and 947,590 women in the age group 20-24 yr, 993,963 men and 942,257 women in the age group 25-29 yr and 467,461 men and 444,503 women in the age group 30-34 yr. No significant differences were found between the observed and expected numbers of cancer of the urinary bladder in the birth cohort 1941-1945 compared with the two other birth cohorts. The relative risk of bladder cancer of the men in the birth cohort 1941-1945 was identical (1.0) with that of the men in the birth cohorts 1931-1935, 1936-1940 and 1931-1940. The relative risk of bladder cancer in the women of the birth cohort 1941-1945 was reduced (0.3) compared with that of the women in the two previous cohorts. The findings indicate that massive intrauterine exposure to saccharin did not involve any risk of cancer of the urinary bladder during the first 20-34 yr of life. (15 Refs) (In DAN)

4. MUTAGENS PRODUCED BY THE PYROLYSIS OF OPIUM AND ITS ALKALOIDS AS POSSIBLE RISK FACTORS IN CANCER OF THE BLADDER AND OESOPHAGUS.

Malaveille C, Friesen M, Camus AM, Garren L, Hautefeuille A, Bereziat JC, Ghadirian P, Day NE, Bartsch H
(c/o Bartsch) Div. Environmental Carcinogenesis, International Agency Res. on Cancer, 150 cours Albert-Thomas, 69372 Lyon, Cedex 8, France
Carcinogenesis; 3(5):577-585 1982

Samples of opium pipe scrapings (opium dross, called sukhteh locally), but not of crude opium, collected in an area with a high incidence of esophageal cancer in north-east Iran, were shown to contain pro-mutagens, producing mostly frameshift mutations in Salmonella typhimurium strains TA1538 and TA98 after metabolic activation. Pyrolysis of opium and of its major alkaloid, morphine, yielded smoke condensates with mutagenic activities 10 and 100x higher, respectively, than that of the sukhteh samples tested. Heterocyclic aromatic hydrocarbons and primary aromatic amines present at different concentrations in these three pyrolysates are considered to be the major active principles. Opium addiction has been implicated as a risk factor in bladder cancer in humans and the ingestion of opium pyrolysates, in conjunction with dietary deficiencies, may be related to the high incidence of esophageal cancer in north-east Iran, although causality has not been established. (Author abstract) (29 Refs)

5. DETERMINATION OF URINARY MUTAGENS IN PATIENTS WITH URINARY TRACT CANCER.

Caderni G, Dolara P, Costantini A, Barbagli G, Calzolai A
Istituto di Farmacologia e Tossicologia, Universita di Firenze, Viale Morgagni 65, I-50134 Firenze, Italy
Eur Urol; 8(4):243-246 1982

The mutagenic activity of urines obtained from patients with urinary tract cancer was measured by the Salmonella/microsome plate test. Smokers and nonsmokers were part of the experimental sample. The urinary mutagenic activity of cancer patients was in the range of the values obtained in the control population. (Author abstract) (8 Refs)

6. AETIOLOGICAL ASPECTS OF BLADDER CANCER IN URINARY BILHARZIA.

Mee AD
Urology Unit, Royal Postgraduate Medical Sch., Hammersmith Hosp., London, England
Saudi Med J; 3(2):123-128 1982

The etiology of urinary bladder cancer (BC) is discussed in relation to bilharzia, the incidence of which is much higher in Egypt than in Saudi Arabia. Beta-glucuronidase in the urine has been linked to BC, increased levels of which occur in patients with urinary infections caused by Escherichia coli and Pseudomonas, which are common causes of secondary infections in urinary bilharziasis. However, experimentally, this enzyme has not been proven to be a significant bladder carcinogen. There is experimental evidence that nitrosamines which may form in the urine of some people produce BC. Variations in dietary nitrate could account for the low incidence of BC in the Arabian peninsula and the higher incidence in Egypt. Egyptian farmers have a higher incidence of BC as a complication of bilharzia than professional and business classes. There was also a greater incidence of nitrosamines in the urine of patients with BC and bilharzia than in patients with other cancers of the bladder alone or in patients with bilharziasis

alone. The results were not conclusive that nitrosamines were the precipitating cause. The possible role of immunocompetence in urinary bilharziasis is discussed. The present study indicates that carcinoma of the bladder in patients with urinary bilharziasis is due to several factors including carcinogens in the urine of the bladder, and depressed immunocompetence caused by schistosoma antigen. (21 Refs)

7. TUMOURS IN ICELAND: 6. TUMOURS OF THE URINARY BLADDER, URETER AND URETHRA. A HISTOLOGICAL CLASSIFICATION AND SOME EPIDEMIOLOGICAL AND ENVIRONMENTAL FACTORS.

Perry SB, Thorhallsson P, Hallgrimsson J
(c/o Thorhallsson, P.) Dept. Pathology, Univ. Iceland, P. O. Box 150, 121 Reykjavik, Iceland
Acta Pathol Microbiol Scand [A]; 90(3):175-183 1982

All primary tumors from the urinary bladder, ureter and urethra submitted for a histological diagnosis in Iceland during the 20 yrs, 1955-1974, and available for review, were typed histologically according to the World Health Organization Classification published in 1973. The series included 237 tumors, and of these 94.5% were from the bladder. Transitional cell carcinomas constituted the largest group, or 120 in males and 77 in females. For transitional cell carcinomas there was a good correlation between growth patterns, grades and pathological stages. Most of the papillary carcinomas were of Grades 1 and 2 and all purely infiltrating carcinomas were of Grade 3. The papillary carcinomas were predominantly superficial and the purely infiltrating were deeply invasive and the degree of cellular anaplasia increased with the depth of invasion from the lamina propria to perivesical tissue and other organs. The incidence of transitional cell carcinoma of the urinary bladder is rising in Icelanders and the incidence in females is the highest reported among European nations. Industrial chemical carcinogens are an unlikely cause of bladder carcinoma in Icelanders but cigarette smoking, and a high consumption of coffee and salted food may play an important role. (Author abstract) (19 Refs)

8. ANALGESICS AND CANCER OF THE RENAL PELVIS IN NEW SOUTH WALES.

McCredie M, Ford JM, Taylor JS, Stewart JH
Renal Unit, Dept. Medicine, Westmead Hosp., Westmead, N.S.W. 2145, Australia
Cancer; 49(12):2617-2625 1982

A lifetime history of analgesic and tobacco consumption was obtained by a questionnaire completed at interview from 67 patients with carcinoma of the renal pelvis (50 women, 27 men) and 180 control subjects drawn from two sources, friends of patients and persons attending a health screening clinic. Regular consumption of analgesics conferred a 10fold relative risk of renal pelvic cancer in women and in men a risk ratio of 4-8. The fraction of cases for which analgesic consumption was an attributable risk was 0.74 in women and 0.43 in men. The effect of tobacco, much less than that of analgesics, was significant only in women (risk ratio approx 4; attributable risk 0.4), and no dose-response relationship was demonstrated. Relative excess risks suggested a synergistic effect when both analgesics and tobacco had been consumed. Standardized risk ratios indicated a dose-response relationship for both phenacetin-containing and non-phenacetin analgesics: moderate consumption doubled the risk of renal pelvic cancer, and heavy consumption increased the risk to 6-16 times that for consumers. (Author abstract) (45 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

9. COMPARATIVE CARCINOGENICITY OF O-TOLUIDINE HYDROCHLORIDE AND O-NITROSOTOLUENE IN F-344 RATS.

Hecht SS, El-Bayoumy K, Rivenson A, Fiala E
Naylor Dana Inst. for Disease Prevention, American Health Foundation, Valhalla, NY, 10595
Cancer Lett; 16(1):103-108 1982

The carcinogenicity of o-toluidine hydrochloride (TOL) and o-nitrosotoluene (NTOL) in F-344 rats was evaluated. Mean weights were somewhat lower in the TOL and NTOL groups than in the control group. The mean daily doses of TOL and of NTOL (administered in the diet) were 0.062 g and 0.051 g, respectively. Food consumption was slightly less in the treated animals than in the animals fed the control diet. NTOL was significantly more effective than TOL in inducing hepatomas and bladder papillomas but was less active in the induction of mammary fibroadenomas. Both compounds induced significant numbers of fibromas of the skin and spleen as well as peritoneal tumors. The sc tumors were fibromas or mammary fibroadenomas. The peritoneal tumors were mesotheliomas and low grade spindle cell sarcomas. All invaded deeply into various abdominal organs and the muscular wall of the cavity. Most liver tumors were highly malignant hepatocarcinomas. Two rats displayed enormous multiple metastases of hepatoma tissue to the lungs. Bladder and pelvis-of-kidney tumors were of the usual transitional epithelium type. These results suggest that N-oxidation is important in the induction of bladder and liver tumors, while other metabolic conversions may play a role in the induction of other tumor types observed. (15 Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

10. PRODUCTION OF KIDNEY TUMORS IN RATS WITH LOW DOSE OF DIMETHYLNITROSAMINE AFTER PARTIAL HEPATECTOMY.

Evarts RP, Brown CA, Mostafa MH
Lab. Carcinogen Metabolism, Div. Cancer Cause and Prevention, NCI, NIH, Public Health Service, U.S. Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 68(2):293-298 1982

The occurrence of kidney tumors in inbred Wistar rats as a result of dimethylnitrosamine (DMN) administration at different intervals after partial hepatectomy was studied. The schedule for DMN administration was determined on the basis of the levels of liver dimethylnitrosamine demethylase (DMN-d) at different intervals after the operation. DMN-d was 62% of the control values at 24 hr, 72% at 72 hr, and 96% at 92 hr after the operation. At these intervals a single dose of DMN (10 mg/kg body wt) was given to partially hepatectomized animals and to untreated controls. At termination, when the animals were 94 wk old, no kidney tumors were found in the control animals, whereas 23 of 54 animals (43%) that had been given injections of DMN 24 hr after partial hepatectomy developed kidney tumors. Kidney tumor incidence was 28 or 12%, respectively, when the carcinogen was administered 72 hr or 92 hr after the operation. The kidney tumor incidence and the ac-

tivity of liver DMN-d were inversely related. (Author abstract) (27 Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

11. ALTERATIONS IN THE SUBCELLULAR DISTRIBUTION OF GUANYLATE CYCLASE AND ITS RESPONSIVENESS TO NITRIC OXIDE IN DIETHYLSTILBESTROL-INDUCED RENAL TUMORS.

Braughler JM, Gilloteaux J, Steggles AW
Dept. Pharmacology, Northeastern Ohio Univ. Coll. Medicine, Rootstown, OH, 44272
Cancer; 50(1):78-84 1982

The cyclic GMP content of diethylstilbestrol-induced renal tumors in the male golden hamster was increased nearly 130-fold over that in kidney from control animals. Cyclic GMP in tumors was 91.80 +-19.18 pmoles cyclic GMP/mg protein compared to 0.72 +-0.07 in control kidneys. Cyclic AMP in tumors was also increased over control, however, to a much lesser degree (2.7-fold). In control kidneys, 84.6% of homogenate guanylate cyclase activity was recovered in the 100,000 x g supernatant fraction. Total homogenate guanylate cyclase activity from diethylstilbestrol-induced renal tumors was increased 5.5-fold over that in control kidneys and only 8.1% was associated with the 100,000 x g supernatant fraction. Neither the soluble or particulate guanylate cyclase from renal tumors could be activated by nitric oxide. The unresponsiveness of tumor guanylate cyclase to nitric oxide was independent of the cation cofactor, and not due to a shift in the dose response curve for nitric oxide. Responsiveness to nitric oxide was not restored by thiols, sugars, other proteins, or hemoglobin. Basal cyclic AMP formation by soluble guanylate cyclase from renal tumors was dramatically increased over that observed in control kidneys, and could not be increased further by nitric oxide. This is the first study of cyclic GMP and guanylate cyclase in a primary estrogen-induced tumor. The possibility that the changes observed in guanylate cyclase from diethylstilbestrol-induced renal tumors are related to in vivo activation of the enzyme by epoxide metabolites of diethylstilbestrol is discussed. (Author abstract) (31 Refs)

12. COVALENT BINDING OF BENZIDINE AND N-ACETYLBENZIDINE TO DNA AT THE C-8 ATOM OF DEOXYGUANOSINE IN VIVO AND IN VITRO.

Martin CN, Beland FA, Roth RW, Kadlubar FF
Cancer Res. Unit, Univ. York, York YO1 5DD, England
Cancer Res; 42(7):2678-2686 1982

Benzidine, a human urinary bladder carcinogen, induces hepatic tumors in mice and rats. In this study [3H]benzidine was administered in drinking water to mice for 1 wk, and the covalent binding of the carcinogen to hepatic DNA was then determined. A single carcinogen: DNA adduct was detected which decreased in concentration by approx 50% at 1 day after treatment and then remained at a nearly constant level for at least 7 days. Injection of radiolabeled benzidine or N-acetylbenzidine into rats also resulted in a single carcinogen:DNA adduct that was chromatographically identical to that obtained in mouse liver. While administration of benzidine and N-acetylbenzidine resulted in high levels of the adduct in rat hepatic DNA, injection of N,N'-[ring-14C]diacetylbenzidine did not give detectable binding. The same carcinogen:DNA adduct found in rat and mouse liver was prepared synthetically by: (a) hydrolysis of calf thymus DNA reacted with N-hydroxy-N'-acetylbenzidine at pH 5; and (b) reaction of N-acetoxy-N,N'-diacetylbenzidine with deoxyguanosine and subsequent selective deacetylation of the product with methanolic ammonia. Mass and nuclear magnetic resonance spectral data of the synthetic products established the structure of the hepatic adduct as N-(deoxyguanosin-8-yl)-N'-acetylbenzidine. The nonacetylated derivative, N-(deoxyguanosin-8-yl)benzidine, was synthesized by carboxylesterase treatment of N-(deoxyguanosin-8-yl)-N'-acetylbenzidine and was shown not to occur in rat and mouse liver DNA. These data indicate that the metabolic activation of benzidine to an ultimate carcinogen in rats and mice does not involve N-hydroxybenzidine or sulfotransferase-catalyzed activation of N-hydroxy-N,N'-diacetylbenzidine. The remaining pathways for metabolic conversion of benzidine to an ultimate carcinogenic species are discussed in relation to liver and urinary bladder carcinogenesis. (46 Refs)

13. NUCLEIC ACID METABOLISM OF BLADDER CARCINOMA CELLS IN VITRO.

Koiso K, Ishii Y, Niijima T
(c/o Niijima) Dept. Urology, Faculty Medicine, Univ. Tokyo, Tokyo, Japan
Urol Res; 10(2):71-74 1982

Nucleic acid metabolism was investigated in bladder carcinoma cells obtained from 27 patients (22 men, 5 women; 40-81 yr old, av 60.1 yr old). Five patients had Grade 1 tumors, 10 Grade 2, and 12 Grade 3. Six patients had Stage A disease, 10 Stage B1, 10 Stage B2, and 1 Stage C. Bladder cancer cells were incubated with 14C-formate or 14C-adenine at 37 C in 95% oxygen and 5% CO2 for 3 hr. Nucleic acids were then extracted and separated, and specific and relative specific activities were calculated. Incorporation of 14C-formate was much higher in Grade III bladder carcinoma cells than in normal epithelium or Grades I and II bladder carcinoma cells. Incorporation rates of 14C-formate into DNA thymine and RNA adenine and guanine were higher in Stage B1 cells than in normal cells; higher rates were also observed for Stage B2 cells. 14C-Adenine incorporation was much higher in bladder carcinoma cells than in normal bladder epithelium. The higher incorporation rates were seen in each base as the grade and stage progressed. The S/N ratio (relative metabolic activities of the de novo nucleic acid synthetic pathway and the salvage pathway) was much higher in bladder carcinoma cells than in normal bladder mucosa, but the differences between grades or stages were not significant. These results indicate that bladder carcinoma cells have greater potential for incorporating nucleic acid precursors than normal bladder epithelium cells; malignant bladder cancer cells appear active in the process of synthesis of nucleic acids, particularly through the salvage pathway. (14 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

14. DNA CONTENT OF HUMAN KIDNEY CARCINOMA CELLS IN RELATION TO HISTOLOGICAL GRADING.

Baisch H, Otto U, Konig K, Kloppel G, Kollermann M, Linden WA
Inst. Biophysics and Radiology, Univ. Hamburg, Hamburg, W. Germany
Br J Cancer; 45(6):878-886 1982

Ploidy and cell-cycle stage were determined by flow cytometry (FCM) in 46 human renal carcinomas. Cell populations with aneuploid DNA were detected in 46% of these. In the investigated samples, the fraction of cells with abnormal DNA content varied from 8 to 100%. The proliferative activity was generally low as indicated by the small fractions of cells in S and (G2 + M) phases. This was confirmed by the labeling indices on autoradiographic slides. The fraction of cells in phases S and (G2 + M) for tumors that were pre-irradiated with 15 or 25 Gy before nephrectomy was only slightly less than in unirradiated tumors. Comparison of the FCM ploidy with the results of histological grading showed that all cases classified as the most malignant Grades IV or IIIB (according to the nuclear and to the combined grading system of Syrjanen and Hjelt (1978)) were hyperdiploid. On the other hand, 45% of the hyperdiploid and 89% of the diploid tumors were of the low Grades I and II. After a follow-up for 6 mo to 2 yr, 8/17 patients with hyperdiploid and only 1/14 patients with diploid tumors have died or relapsed with multiple metastases. The results indicate that the aneuploidy of tumors, measured by FCM, might provide useful additional information for prognosis. (Author abstract) (14 Refs)

15. KARYOTYPE ALTERATIONS IN CARCINOMA OF THE URINARY BLADDER CORRELATED WITH DEGREE OF MALIGNANCY AND DEPTH OF INFILTRATION (MEETING ABSTRACT).

Harbott J, Burk K
Urologische Universitatsklinik, Marburg, W. Germany
Adriamycin. Symposium, March 12-13, 1981, Frankfurt, W. Germany. Arbeitsgemeinschaft Internistische Onkologie 46 pp, 1981.

Cytologic studies quite often reveal changes in the ploidies of bladder carcinoma cells. As a rule chromosomes which differ in shape from those of the normal human karyotype, the so-called marker chromosomes, are also found in the nuclei of these cells. The results of karyotyping are correlated with the histological findings of the tumor-nodes-metastasis (TNM) classification. The occurrence of marker chromosomes and the deviations from the diploid chromosome complement seem to provide some indications as to the further behavior of the tumor. (no Refs) (In GER)

16. BACKSCATTERED ELECTRON IMAGING BY SEM OF NORMAL AND NEOPLASTIC URINARY BLADDER (MEETING ABSTRACT)

Smith GP, Williams AE
Teaching and Research Centre, University of Edinburgh, Western General Hospital, Edinburgh, Scotland
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

The study of urinary bladder cancer by scanning electron microscopy (SEM) has concentrated on the changes in luminal surface structure and organization during neoplasia. However, SEM backscattered electron imaging (BSE) of tissues stained with heavy elements such as silver allows visualization of subsurface structures. This method was used to examine normal and carcinogen treated rat bladders, and biopsies from patients under investigation for bladder cancer. Results show a predominance of binucleate superficial cells in the bladders of normal rats, and an organizational relationship between the superficial layer of cells and the underlying intermediary cell nuclei suggestive of the proliferative unit organization seen in epidermis. In rat bladders treated with methylnitrosourea, changes were observed in intracellular organization before urothelial changes could be observed histologically and by SEM examination of surface topology; superficial cells became predominantly uninuclear and the relationship between superficial and intermediary cells was lost. Areas where these changes have occurred can be readily observed at low magnifications. Preliminary observations of human biopsy material suggest that similar organizational and neoplastic changes occur. (3 Refs)

17. IN VITRO CHARACTERIZATION OF FOUR N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL] FORMAMIDE (FANFT) INDUCED MOUSE BLADDER TUMORS.

Mickey DD, Mickey GH, Murphy WM, Niell HB, Soloway MS
Dept. Urology, Univ. Tennessee, Center Health Sciences, 956 Court Ave., Box 10, Memphis, TN, 38163
J Urol; 127(6):1233-1237 1982

Four long-term murine bladder tumor cell lines were established in vitro. The four lines were initiated from primary N-[4-(5-nitro-2-furyl)-2-thiazolyl] formamide (FANFT)-induced murine bladder tumors arising in C3H/He mice. Each was maintained as a solid tumor in syngeneic mice for at least 30 generations before initiation in tissue culture. The cell lines MBT-2, MBT-8, MBT-409, and MBT-683, have been subcultured over 75x in vitro for 18 mo. They are all epithelial, grow in islands on plastic Petri dishes before confluent growth and form colonies in soft agar suspension culture. Morphologic studies indicate that all four lines have epithelial characteristics and karyotypic studies indicate that all lines have polyploidy and marker chromosomes. Population doubling times range from 10 to 26 hr and are consistent for each line. (Author abstract) (27 Refs)

18. THE EFFECT OF CHEMICALLY DEFINED SERUM-FREE MEDIUM ON CELL LINES OF HUMAN RENAL CANCER: PROPAGATION, GROWTH REQUIREMENTS, AND TUMORIGENICITY (MEETING ABSTRACT).

Clayman RV, Noreen D, Beck S, Fraley EE
University of Minnesota, 420 Delaware Street S. E., Minneapolis, MN, 55455
In Vitro; 18(3,part2):306 1982

Biochemical studies of human renal cell cancer (RCC) have been hampered by the lack of a chemically defined, serum-free medium (SFM). Herein we report the growth of two cell lines of human RCC on a form of SFM developed by Taub. Four cell lines of human RCC were studied: 786-0, 769-P, 1072-F, and Caki-1. Twelve-day growth curves were obtained for each line using: SFM, serum-containing medium (SCM), and a control medium. In addition, cells propagated on SFM were subcultured, plated on agar, and also inoculated into athymic mice. Finally, hormonal-exclusion studies were performed with hydrocortisone, prostaglandin E1, insulin, transferrin, and triiodothyronine. Only 786-0 and Caki-1 had similar growth rates on SFM and SCM. The plating efficiency on SFM was 30-

50% less than on SCM. The hormonal-exclusion studies revealed transferrin, hydrocortisone, and insulin essential factors for 786-0 and insulin to be the only necessary factor for Caki-1. Following growth on SFM, both cell lines continued to produce colonies in agar and Caki-1 also produced tumors in athymic mice. To date, 786-0 and Caki-1 have been maintained in continuous culture on SFM for more than 7 months and have undergone 10 and 13 passages, respectively. (no Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

19. A, B, H ANTIGEN DETECTABILITY IN NORMAL AND NEOPLASTIC UROTHELIUM. INFLUENCE OF METHODOLOGIC FACTORS.

Limas C, Lange P
Dept. Lab. Medicine and Pathology, Veterans Admin. Medical Center, 54th St. and 48th Ave. South, Minneapolis, MN, 55417
Cancer; 49(12):2476-2484 1982

Markedly reduced or absent reactivity for the normally expressed A B H antigens in transitional cell carcinomas (TCCs) of the human urinary bladder appears to correlate with an aggressive clinical course. To evaluate the clinical applicability of this observation, the authors investigated the influence of methodologic variants as well as certain patient characteristics on urothelial A, B, H reactivity. Biopsy-obtained TCCs and/or normal mucosae from 104 patients were examined for the effect of fixation, paraffinization, and alcohol treatment. Variability due to the secretor status and blood group of the patient was evaluated in conjunction with methodologic factors. In the fresh-frozen state, the expected antigen was always detectable in normal mucosas but only in 69% of TCCs regardless of patient's secretor status and blood group (BG). Few normal mucosae (12%) but a large number of TCCs (46%) converted to negative after paraffin processing. Similar reduction in A, B, H reactivity was also noted when the tissues were treated with concentrations of alcohol comparable to those used in the paraffin procedure. Tumor antigens were more sensitive to alcohol. This suggested that in neoplastic cells ABH determinants are not only fewer but also disproportionately represented on polar (alcohol-soluble) molecules. Alcohol more profoundly affected tissues from nonsecretors probably because the proportion of alcohol-soluble A, B, H substances differs in secretors and nonsecretors. In the fresh-frozen state, the H antigen was detectable with the Ulex Europeus lectin in the majority of TCCs from BGO patients (79%) as well as in most tumors from BGA or B patients (90%) even in the absence of the expected A or B antigen. Alcohol treatment, however, more potently reduced reactivity for H rather than the other antigens, a phenomenon that also points to the significance of glycolipid extraction and explains the marked differences in the detectability of this antigen between fresh-frozen and paraffin-processed TCCs. (Author abstract) (24 Refs)

20. BLOOD GROUP PRECURSOR T-ANTIGEN EXPRESSION IN HUMAN URINARY BLADDER CARCINOMA.

Coon JS, Weinstein RS, Summers JL
Dept. Pathology, Rush-Presbyterian-St. Luke's Medical Center, 1753 W. Congress Parkway, Chicago, IL, 60612
Am J Clin Pathol; 77(6):692-699 1982

Tumor deletion of the ABH blood group antigens (BGAg) heralds an unfavorable prognosis in human bladder cancer. The T antigen (Thomsen-Friedenreich antigen: TAg), a precursor of other BGAg, has previously been found in malignant but not most normal cells, in which the TAg is cryptic but can be unmasked with neuraminidase (NMD). We investigated the prognostic significance of TAg expression in bladder cancer by staining paraffin sections with a T-specific lectin (peanut agglutinin [PNA]) immunoperoxidase technic. Seventy-two cases of low grade, low stage bladder cancer, 21 cases of high grade bladder cancer, and 68 controls were studied. All normals expressed the TAg only after NMD treatment (Cryptic TAg+). The Grade III cancers, all invasive, either expressed the TAg (TAg+) (67%) or lacked T even after NMD (Cryptic TAg-) (29%), indicating that the T structure was lost rather than masked as in normal tissue. Thirty-nine percent of 23 Grade I and II cancers which were TAg+ or Cryptic TAg- subsequently became invasive (Stage B), compared with 10% of 49 Cryptic TAg+ cancers. For 32 Grade I and II, ABH BGAg negative cancers, 64% of TAg+ or Cryptic TAg- cancers became invasive, compared with 17% of cancers which had Cryptic TAg+. Thus, the TAg may be a prognostically useful immunohistochemical tumor marker in bladder cancer, especially for tumors negative for ABH BGAg. (Author abstract) (37 Refs)

21. THE DETECTION OF BLOOD GROUP ISOANTIGEN ON SUPERFICIAL BLADDER TUMOURS USING MONOCLONAL ANTIBODIES AND IT'S VALUE IN PREDICTING SUBSEQUENT INVASIVE RECURRENCE (MEETING ABSTRACT)

Finan PJ, Lennox ES, Bleehen NM
MRC Clinical Oncology Unit, Cambridge, England
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh, Scotland. British Association for Cancer Research 78 pp., 1982.

It has been claimed that loss of normally occurring blood group isoantigen (BGI) on malignant transitional epithelium is a reliable predictor of subsequent invasive recurrence. Previous workers have used the specific red cell adherence test together with conventional antisera. However, problems have been encountered both with the technique and reproducibility of results. We have therefore investigated a more direct method of demonstrating the presence of BGI on normal and malignant transitional epithelium. Using an indirect immunoperoxidase technique and monoclonal antibodies to the blood groups A and B. BGI was detected on paraffin sections of normal urothelium from 14 patients. On initial biopsies from 39 patients with superficial bladder tumors, followed for 5 years or until muscle invasion occurred, BGI was detected in 31. The rate of invasive recurrence in the isoantigen-negative group was significantly higher than in the isoantigen-positive group. (3 Refs)

22. TRANSFORMING GENES OF HUMAN BLADDER AND LUNG CARCINOMA CELL LINES ARE HOMOLOGOUS TO THE RAS GENES OF HARVEY AND KIRSTEN SARCOMA VIRUSES.

Der CJ, Krontiris TG, Cooper GM
Sidney Farber Cancer Inst., Boston, MA, 02115
Proc Natl Acad Sci USA; 79(11):3637-3640 1982

Blot hybridization analysis indicated that NIH 3T3 mouse cells transformed by high mol wt DNAs of a human bladder and a human lung carcinoma cell line contained new sequences homologous, respectively, to the transforming genes of Harvey (rasH) and Kirsten (rasK) sarcoma viruses. The unique ras sequences were present in multiple independent NIH cell lines

ansformed in both primary and secondary transfection assays nd corresponded to ras sequences normally present in human)NAs. The ras gene product was expressed in NIH cells trans- ormed by bladder carcinoma DNAs and in the human bladder arcinoma cell lines at levels two- to four-fold greater than the evel observed in nontransformed NIH 3T3 cells. These results ndicate that the transforming genes of these human tumor cell nes are the cellular homologs of two retroviral transforming enes. (Author abstract) (30 Refs)

3. HUMAN EJ BLADDER CARCINOMA ONCOGENE IS HOMOLOGUE OF HARVEY SARCOMA VIRUS RAS GENE.

Parada LF, Tabin CJ, Shih C, Weinberg RA
Center for Cancer Res., Dept. Biology, Massachusetts Inst. Technology, Cambridge, MA, 02139
Nature; 297(5866):474-478 1982

Examination of homologies between retroviral oncogenes nd transforming sequences defined by transfection reveals that he human bladder carcinoma (EJ) oncogene is homologous to he Harvey sarcoma virus oncogene (ras). Structural analysis imits the region of homology to a 3.0-kilobase SacI fragment of the EJ oncogene. Both EJ and ras DNA probes detect simiar transcripts in transfectants derived from bladder carcinoma ell lines. (Author abstract) (42 Refs)

24. THE ONCOGENIC CIRCLE CLOSES.

Rigby PW
Imperial Coll. Science and Technology, London SW7 2BZ, England
Nature; 297(5866):452-453 1982

Characterization of cellular oncogenes is reviewed. Oncogenes exhibit target specificity within a lineage. Recombinant DNA technics have been applied to the cloned human bladder carcinoma oncogene. The relationship between cellular oncogenes and proto-oncogenes (genes detected by transfection) has been studied. Retrovirus onc genes have been cloned and used to analyze DNA of NIH cells transformed by a variety of cellular oncogenes. The cloned human bladder carcinoma oncogene has been shown to be homologous to ras, the transforming gene of Harvey murine sarcoma virus. Mechanisms of oncogene activation and action are discussed. (19 Refs)

25. ISOLATION OF A TRANSFORMING SEQUENCE FROM A HUMAN BLADDER CARCINOMA CELL LINE.

Shih C, Weinberg RA
Dept. Molecular Biology, Massachusetts General Hosp., Boston, MA, 02139
Cell; 29(1):161-169 1982

We have isolated the component of human bladder carcinoma cell DNA that is able to transform mouse fibroblasts. The oncogenic sequence was isolated initially from a lambda phage genomic library made from DNA of a transfected mouse cell carrying the human oncogene. A subcloned insert of 6.6 kb that carried transforming activity was amplified in the plasmid vector pBR322. The subcloned oncogene has been used as a sequence probe in Southern blot analyses. The oncogene appears to derive from sequences present in normal cellular DNA. Structural analysis has failed so far to reveal differences between the oncogene and its normal cellular homolog. The oncogene is unrelated to transforming sequences detected in a variety of other types of human tumor cell lines derived from colonic and lung carcinoma and from neuroblastoma. In contrast, the EJ bladder oncogene appears closely related to one that is active in the human T24 bladder carcinoma cell line. The oncogene appears to have undergone little, if any, amplification in several bladder carcinoma cell lines. (Author abstract) (35 Refs)

REVIEWS AND OTHER RELATED STUDIES

26. HUMAN BLADDER TUMOURS IN SHORT TERM ORGAN CULTURE (MEETING ABSTRACT)

Lawson AH, Riches AC, Weaver JP
Department of Anatomy and Experimental Pathology, University of St. Andrews, St. Andrews, Scotland
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh Scotland. British Association for Cancer Research 78 pp., 1982.

Transitional Cell Tumors of the Urinary Bladder present a problem in management because of their tendency to recur. The tumors may be completely cured after resection, may recur at the same grade and stage or may recur at a worsening grade and stage. There is no way of predicting behavior on histological appearances alone. Treatment may be by resection, radiotherapy, total cystectomy, intravesical chemotherapy or systemic chemotherapy. Diffuse papillary carcinomas are particularly difficult to treat by resection but total cystectomy or radiotherapy carries a high morbidity for a low grade tumor. These may be treated by instilling anticancer agents into the bladder. Human bladder tumors have been maintained in organ culture and their kinetic properties and responses to anti-cancer agents in vitro have been studied. Proliferative behavior is studied using 125I-iododeoxyuridine uptake in combination with histology, vincristine sulphate metaphase arrest and autoradiography with tritiated thymidine. Drug treatment is mimicked by immersing the explants for 1 hour, washing and then studying recovery. Different behavior is seen in different grades of tumor and different tumors respond differently to different drugs. Correlation between 'in vitro' and 'in vivo' behavior remains to be established. If a method of identifying tumors liable to rapidly progress could be established it would enable urologists to embark on much more radical treatment at an early stage in the disease. (no Refs)

27. THE GROWTH OF HUMAN BLADDER CANCER BIOPSIES IN IMMUNE-DEPRIVED MICE (MEETING ABSTRACT)

Hay JH, Busuttil A, Steel CM, Duncan W
University Department of Clinical Oncology, Western General Hospital, Edinburgh, Scotland
Twenty-third Annual General Meeting of the British Association for Cancer Research, March 29-31, 1982, Edinburgh Scotland. British Association for Cancer Research 78 pp., 1982.

A series of serially transplantable xenografts has been successfully established from biopsies of transitional cell carcinoma of the bladder. These are now being used for chemotherapeutic and radiobiological studies. CBA/Lac mice were prepared by thymectomy and whole body irradiation following pre-treatment with 200 mg/kg of cytosine arabinoside. The mice received 750 cGy of 250 kV x-rays, which is the LD50 of untreated mice from our colony. All biopsy material has been collected from primary bladder tumors, no metastatic tumor has been used. To date a total of 4/33 transitional cell carcinoma biopsies have taken and been successfully passaged. Zero of eight well differentiated (G1), 2/12 moderately differentiated (G2) and 2/13 poorly differentiated (G3) tumors have taken.

One squamous carcinoma and one mixed transitional cell and adenocarcinoma have failed to grow. Three of four successful takes have been from tumor recurring after surgical resection, the fourth was from a previously untreated patient. Three of four of the xenografts grow subcutaneously as approximately spherical tumor nodules, the other maintains the sessile pattern commonly seen in the bladder. The histological appearances of all the xenografts are similar to those of their parent tumors. No successful takes have occurred from biopsies taken when the bladder was irrigated with water or from biopsies taken with the resectoscope. (1 Ref)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. TOXICITY OF POLYBROMINATED BIPHENYLS (PBBS) IN DOMESTIC AND LABORATORY ANIMALS.
Damstra T, Jurgelski W, Posner HS, Vouk VB, Bernheim NJ, Guthrie J, Luster M, Falk HL
Natl. Inst. Environmental Health Sciences, Post Office Box 12233, Research Triangle Park, NC, 22709
Environ Health Perspect; 44():175-188 1982

2. CHLOROFORM: A REVIEW OF ITS METABOLISM, TERATOGENIC, MUTAGENIC, AND CARCINOGENIC POTENTIAL.
Davidson IW, Sumner DD, Parker JC
(c/o Parker) ECAO, Environmental Protection Agency, MD-52, Research Triangle Park, MD, 27711
Drug Chem Toxicol; 5(1):1-87 1982

3. FORMALDEHYDE IN PRESENT-DAY ENVIRONMENTAL TOXICOLOGY.
Beritic T, Kovac S, Dimov D
Odjel za profesionalne bolesti, Institut za medicinska istrazivanja i medicinu rada, Zagreb, Yugoslavia
Arh Hig Rada Toksikol; 32(4):363-395 1981
In SCR

4. HORMONES AS ETIOLOGICAL AGENTS IN NEOPLASIA.
Furth J
Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

5. CURRENT VIEWS ON HORMONES AND BREAST CANCER.
Molinatti GM, Limone P
Cattedra di Endocrinologia, Universita di Torino, C.so Polonia, 14, 10126 Turin, Italy
Minerva Med; 73(17):1047-1053 1982
In ITA

6. THE CHROMOSOMAL EFFECTS OF THE ORAL CONTRACEPTIVE.
Bishun NP
Tissue Culture and Cytogenetics Unit, Res. Dept., Marie Curie Memorial Foundation, The Chart, Oxted, Surrey, England
J Surg Oncol; 20(2):115-118 1982

7. TOXICITY AND CARCINOGENICITY OF NICKEL AND ITS COMPOUNDS. A REVIEW OF THE CURRENT STATUS.
Raithel HJ, Schaller KH
Institut fur Arbeits- und Sozialmedizin, Poliklinik fur Berufskrankheiten, Universitat Erlangen-Nurnberg, Schillerstrasse 25-29, D-8520 Erlangen, W. Germany
Zentralbl Bakteriol Mikrobiol Hyg [B]; 173(1/2):63-91 1981
In GER

8. HISTORICAL OVERVIEW OF NITROSOUREA DEVELOPMENT.
Goldin A
Div. Cancer Treatment, NCI NIH, Building 37, Room 5E20, Bethesda, MD, 20205
INSERM Symp; 19:3-11 1981

9. PATHOLOGY.
Goyer RA
Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC
JAMA; 247(21):2973-2975 1982

RADIATION CARCINOGENESIS

10. IDENTIFYING THE HEALTH RISKS FROM VERY LOW-DOSE SPARSELY IONIZING RADIATION.
Dreyer NA, Friedlander E
Epidemiology Resources, Inc., P.O. Box 57, Chestnut Hill, MA, 02167
Am J Public Health; 72(6):585-588 1982

11. RISK OF RADIOLOGICAL EXAMINATIONS.
Jankowski J
Instytut Medycyny Pracy w Lodzi, ul. Olowiana 6, 91-614 Lodz, Poland
Pol Przegl Radiol; 45(6):383-386 1981
In POL

12. RADIOBIOLOGY OF RISK ESTIMATES IN MEDICAL IRRADIATION (MEETING ABSTRACT)
Ross HH
Columbia University, New York, NY
IN: 148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.

13. RADIATION-INDUCED VASCULAR INJURY AND ITS RELATION TO LATE EFFECTS IN NORMAL TISSUES.
Law MP
MRC Cyclotron Unit, Hammersmith Hosp., London W12 OHS, England
Adv Radiat Biol; 9:37-73 1981

14. CURRENT CONCEPTS IN ULTRAVIOLET CARCINOGENESIS.
Granstein RD, Sober AJ
(c/o Sober) Dept. Dermatology, Massachusetts General Hosp., Boston, MA, 02114
Proc Soc Exp Biol Med; 170(2):115-125 1982

15. METABOLIC CHANGES AFTER EXPOSURE TO RADIONUCLIDES.
Kalistratova VS
No affiliation given
Med Radiol (Mosk); 27(4):62-71 1982
In RUS

DIETARY FACTORS IN CARCINOGENESIS

16. CAFFEINE: AN UPDATE.
Ames BL, Ford RA
Bernard L. Ames and Associates, 108-18 Queens Blvd., Forest Hills, NY, 11375
Drug Chem Toxicol; 4(4):311-329 1981

17. ANALYSIS OF MUTAGENIC EFFECTS OF FOREIGN SUBSTANCES IN THE FOOD PRODUCTS.
Maganova NB
Inst. Nutrition, Moscow, USSR
Vopr Pitan; (2):3-8 1982
In RUS

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

18. RADIATION EPIDEMIOLOGY (MEETING ABSTRACT)
Marks S
No affiliation given
148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.

19. EPIDEMIOLOGICAL STUDIES ON RADIATION CARCINOGENESIS IN HUMAN POPULATIONS FOLLOWING ACUTE EXPOSURE: NUCLEAR EXPLOSIONS AND MEDICAL RADIATION.
Fabrikant JI
Donner Lab., Univ. California, Berkeley, CA, 94720
Yale J Biol Med; 54(6):457-469 1981

20. EPIDEMIOLOGIC APPROACH TO CANCER.
Guinee VF
Dept. Epidemiology, Univ. Texas System Cancer Center, M.D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

21. EPIDEMIOLOGY AND EARLY DETECTION OF CANCER OF THE ESOPHAGUS.
Sorouri P
900 Hillside Road, Wilmington, DE, 19807
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

22. METABOLIC EPIDEMIOLOGY OF LARGE BOWEL CANCER.
Hill MJ
Central Public Health Lab., Colindale Ave., London NW9, England
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

23. EPIDEMIOLOGY OF GASTRIC CANCER AND ITS PRECURSOR LESIONS.
Correa P
Louisiana State Univ. Medical Center, New Orleans, LA, 70112
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

24. TRENDS IN THE INCIDENCE OF GASTRIC CARCINOMA (MEETING ABSTRACT)
Nobrega FT
Preventive and Internal Medicine, Mayo Clinic, Rochester, MN
Eleventh Annual William Beaumont Gastrointestinal Symposium, March 24-26, 1982, El Paso, Texas. William Beaumont Army Medical Center 56 pp., 1982.

25. CANCER IN INFLAMMATORY BOWEL DISEASE.
Bayless TM, Yardley JH
Johns Hopkins Hosp., Baltimore, MD, 21205
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

26. GENETIC ASPECTS OF GUT CANCER.
McConnell RB
Broadgreen Hosp., Liverpool, England
Gastrointestinal Cancer 1. Decosse JJand Sherlock P, ed. The Hague, Martinus Nijhoff Publishers, Cancer Treatment and Research, Vol. 3, 452 pp., 1981.

27. HOST AND ENVIRONMENTAL FACTORS ENHANCING CARCINOGENESIS IN THE RESPIRATORY TRACT.
Nettesheim P, Topping DC, Jamashi R
Natl. Inst. Environmental Health Sciences, Research Triangle Park, NC, 27709
Annu Rev Pharmacol Toxicol; 21:133-163 1981

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28. A SEARCH FOR SAFE DRINKING WATER.
Hairsine MA, Schumm HA
Northern Indiana Health Systems Agency, Inc., South Bend, IN
A Search for Safe Drinking Water. Available from National Technical Information Service, Springfield, VA, as HRP-0903845/6, 68 pp., 1981.

29. OCCUPATIONAL EXPOSURES TO URANIUM: PROCESSES, HAZARDS, AND REGULATIONS.
Stoetzel GA, Fisher DR, McCormack WD, Hoenes GR, Marks S
Battelle Pacific Northwest Lab., Richland, WA
Occupational Exposures to Uranium: Processes, Hazards, and Regulations. Available from National Technical Information Service, Springfield, VA, as PNL-3341-USUR-01., 91 pp., 1981.

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

30. THE ROLE OF RADIATION AND CHEMICALS IN THE INDUCTION OF MUTATIONS AND EPIGENETIC CHANGES DURING CARCINOGENESIS.
Trosko JE, Chang CC
Dept. Human Development, Coll. Human Medicine, Michigan State Univ., East Lansing, MI, 48824
Adv Radiat Biol; 9:2-36 1981

31. SOME EFFECTS OF CARCINOGENS ON CELL ORGANELLES.
Svoboda DJ, Reddy J
Dept. Pathology and Oncology, Univ. Kansas Coll. Health Sciences, Kansas City, KS
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

32. CHEMICAL CARCINOGENESIS: INTERACTIONS OF CARCINOGENS WITH NUCLEIC ACIDS.
Rajalakshmi S, Prema M, Sarma D
Dept. Pathology, Univ. Toronto, Toronto, Ontario, Canada
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33. A MOLECULAR RATIONALE FOR NITROSOUREA INDUCED CYTOTOXICITY.
Tew KD
Lombardi Cancer Center, Div. Medical Oncology, Georgetown Univ., 3800 Reservoir Road, N.W., Washington, DC, 20007
INSERM Symp; 19:61-77 1981

34. MODIFICATION OF DNA AND RNA BASES BY THE NITROSOUREAS.
Ludlum DB, Tong WP
Div. Oncology, Dept. Pharmacology and Experimental Therapy, Albany Medical Coll., Albany, NY, 12208
INSERM Symp; 19:21-31 1981

35. CALMODULIN AND CA2+ IN NORMAL AND TRANSFORMED CELLS.
Vogel ML, Sedwick WD, Vanaman TC
Dept. Microbiology and Immunology, Duke Univ. Medical Center, Durham, NC, 27710
Fed Proc; 41(7):2283-2288 1982

36. METABOLISM AND TOXICITY OF AFLATOXINS.
Hsieh DP, Wong JJ
Dept. Environmental Toxicology, Univ. California, Davis, Davis, CA, 95616
Adv Exp Med Biol; 136(partB):847-863 1982

37. REACTION OF MICROSOMAL AND CYTOSOLIC ENZYMES WITH N-ARYLACETOHYDROXAMIC ACIDS IN THE PRESENCE OF OXYGEN.
Lenk W, Scharner U
Pharmakologisches Institut, Universitat Munchen, Nussbaumstrasse 26, D-8000 Munchen 2, W. Germany
Adv Exp Med Biol; 136(partB):951-970 1982

38. METABOLIC ACTIVATION AND DEACTIVATION MECHANISMS OF DI-, TRI-, AND TETRACHLOROETHYLENES.

Henschler D, Hoos R

Inst. Toxicology, Univ. Wurzburg, Versbacher Strasse 9, Wurzburg D-8700, W. Germany

Adv Exp Med Biol; 136(partA):659-666 1982

39. METABOLIC ACTIVATION AND HEPATOTOXICITY OF TRICHLOROETHYLENE.

Reynolds ES, Moslen MT

Chemical Pathology Lab., Dept. Pathology, Univ. Texas Medical Branch, Galveston, TX

Adv Exp Med Biol; 136(partA):693-701 1982

40. THE ACTIVATING ROLE OF GLUTATHIONE IN THE MUTAGENICITY OF 1,2-DIBROMOETHANE.

van Bladeren PJ, Breimer DD, Rotteveel-Smijs GM, Hoogeterp JJ, Mohn GR, De Groot A, Van Zeeland AA, Van der Gen A

Dept. Pharmacology, Univ. Leiden, P.O. Box 9502, 2300 RA Leiden, The Netherlands

Adv Exp Med Biol; 136(partA):809-820 1982

41. METABOLISM OF POLYCYCLIC AROMATIC HYDROCARBONS IN PLACENTA.

Juchau MR, Chao ST, Namkung MJ

Dept. Pharmacology, Sch. Medicine, SJ-30, Univ. Washington, Seattle, WA, 98195

Adv Exp Med Biol; 136(partA):555-573 1982

MODIFICATION OF CARCINOGENESIS

42. THE INTESTINAL ENZYMATIC BIOTRANSFORMATION SYSTEM: POTENTIAL ROLE IN PROTECTION FROM COLON CANCER.

Hoensch HP, Hartmann F

Medizinische Universitatsklinik, D-7400 Tubingen, W. Germany

Hepatogastroenterology; 28(4):221-228 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

43. THE ONCOGENIC CIRCLE CLOSES.

Rigby PW

Imperial Coll. Science and Technology, London SW7 2BZ, England

Nature; 297(5866):451-453 1982

44. ANALYSIS OF CASES OF HEPATIC CELL CARCINOMA THAT TRANSFORMED FROM VIRAL HEPATITIS.

Ichida F, Honma A, Soga K

Third Dept. Internal Medicine, Niigata Univ. Sch. Medicine, Niigata, Japan

Nippon Rinsho; 40(2):468-477 1982

In JPN

45. ROLE OF VIRUSES IN THE INDUCTION OF PRIMARY INTRACRANIAL TUMORS.

Walsh JW, Zimmer SG, Perdue ML

Div. Neurosurgery, Univ. Kentucky Medical Center, 800 Rose St., Lexington, KY, 40536

Neurosurgery; 10(5):643-662 1982

METHODOLOGY IN CARCINOGENESIS RESEARCH

46. TRANSLATION OF PHARMACOKINETIC/ BIOCHEMICAL DATA INTO RISK ASSESSMENT.

Dietz FK, Reitz RH, Watanabe PG, Gehring PJ

Toxicology Res. Lab., Health and Environmental Sciences, Dow Chemical, 1803 Building, Midland, MI, 48640

Adv Exp Med Biol; 136(partB):1399-1424 1982

47. IN VITRO ASSAYS FOR THE DIFFERENTIATION OF TUMOR PROMOTORS FROM CARCINOGENS AFTER ROUTINE CARCINOGENESIS BIOASSAYS (MEETING ABSTRACT)

Ward JM, Rice JM

Frederick Cancer Research Center, Frederick, MD

Second Annual Meeting of the Society of Environmental Toxicology and Chemistry, November 22-25, 1981, Arlington, Virginia. Society of Environmental Toxicology and Chemistry 150 pp., 1982.

48. ENVIRONMENTAL CARCINOGENS: SELECTED METHODS OF ANALYSIS. VOLUME 4. SOME AROMATIC AMINES AND AZO DYES IN THE GENERAL AND INDUSTRIAL ENVIRONMENT.

Egan H, Fishbein L, O'Neill IK, Castegnaro M, Bartsch H

Lab. Government Chemist, London, England

IARC Sci Publ (40): 347 pp., 1981.

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PHILIP C. HANAWALT Stanford University	*Cellular Responses to Damaged DNA*	#VK03 54 min.
CHARLES HEIDELBERGER University of Southern California	*Mutagenesis and Oncogenic Transformation of Mouse Embryo Cells*	#VK04 54 min.
FRED RAPP Milton S. Hershey Medical Center	*The Interaction of Herpesviruses and Host Cells Leading to Latency or Transformation*	#VK05 52 min.
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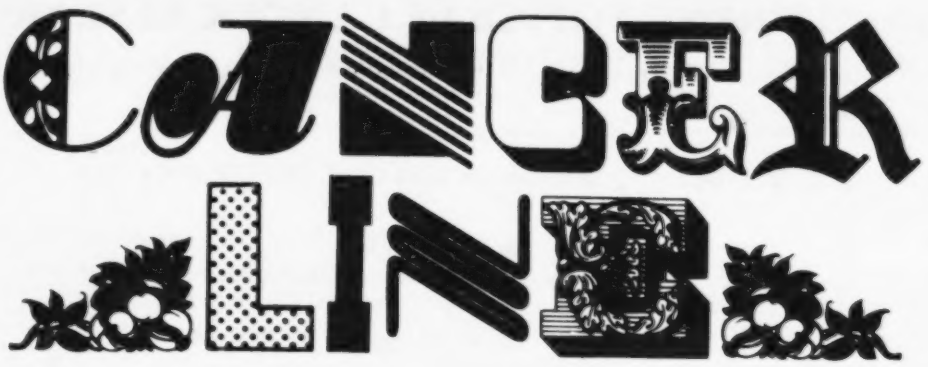

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ICRDB CANCERGRAM

ORGAN SITE CARCINOGENESIS

Kidney and Urinary Tract

SERIES CK17 No. 82/12

DECEMBER, 1982

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PREVALENCE OF URINARY TRACT CANCER IN HUMAN POPULATIONS

1. A PROPORTIONATE MORTALITY STUDY OF AN OIL, CHEMICAL AND ATOMIC WORKERS LOCAL IN TEXAS CITY, TEXAS.

Reeve GR, Thomas TL, Kelly VF, Waxweiler RJ, Itaya S
Biometry Section, Industrywide Studies Branch, Natl. Inst. for Occupational Safety and Health, Robert A. Taft Laboratories, Cincinnati, OH, 45226

Ann NY Acad Sci; 381:54-61 1982

A proportionate mortality ratio (PMR) study was conducted of deceased members of the Oil, Chemical and Atomic Workers Union in Texas City, Texas in order to determine whether unusual patterns of cancer mortality exist in petrochemical plants and refineries. A total of 264 white union members who died after 1947 were included in the study, and two refineries (A and B) were analyzed in depth. In Refinery A, the PMR for nonmotor vehicle accidents was elevated (12 deaths observed vs 7.36 expected) and that for all cancer was only slightly elevated (1.18). However, excess deaths from skin cancer (PMR = 7.88), brain and CNS neoplasms (4 observed

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vs 1.57 expected), kidney cancer (2 observed vs 0.84 expected), and liver cancer (3 observed vs 0.64 expected) were observed. In Refinery B, excess deaths from lung cancer (6 observed vs 3.86 expected; not statistically significant) and hematopoietic and lymphatic cancer (4 observed vs 1.22 expected) were observed. Thus, deaths due to skin, brain, liver, and kidney cancer at Refinery A and deaths due to hematopoietic and lymphatic cancer at Refinery B were proportionately in excess. The relative excess of melanoma deaths observed at Refinery A appears to represent an occupationally related health problem. The relative excess of other cancer deaths at these refineries warrant further study. (18 Refs)

2. THE RISK OF UPPER URINARY TRACT TUMOR IN PATIENTS WITH BLADDER CARCINOMA (MEETING ABSTRACT).

Mechali P, Correa RJ
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

It is a prevalent opinion that patients with bladder tumors (BT) are at high risk for developing transitional cell upper urinary tract tumors (UTT). As a corollary, it is an accepted practice to do repeated routine IVP to monitor for the appearance of such tumors. We undertook the current study in order to test the validity of that approach. First, we analyzed the charts of 382 patients referred to the Mason Clinic for bladder tumor, between 1943 and 1971, and followed up for 10 years or more, or until their death. BT preceded UTT concomitant 1/382-BT and UTT concomitant 1/382. BT occurred after UTT was diagnosed: 7/382. No UTT 373/382. Second, we looked at 52 patients referred to the Mason Clinic for upper urinary tract transitional cell tumors between 1943 and 1981, an overlapping but not identical population: BT before UTT: 2/52-BT and UTT concomitant 5/52 (one subsequently recurred) - BT after UTT: 12/52. No BT 33/52. The incidence of 3.8% of UTT preceded by BT is impressive, but one has to observe that this reflects the referral bias of a large institution (which is more likely to publish and set trends in the practice of urology). On the other hand, only .26% of BT were found to be followed by UTT. This suggests that in unselected BT, it may not be indicated to do repeated routine IVP in otherwise asymptomatic patients to screen for UTT. (no Refs)

ETIOLOGICAL FACTORS IN HUMAN URINARY TRACT CARCINOGENESIS

3. IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS: THE RUBBER INDUSTRY.

IARC Working Group
Div. Environmental Carcinogenesis, International Agency for Res. on Cancer, Lyon, France
IARC Monogr Eval Carcinog Risk Chem Hum 28: 486 pp., 1982.

The carcinogenic risks of exposures to workers in the rubber industry is evaluated. Manufacturing of tires, and other rubber goods are considered with respect to exposures incident to the mixing of elastomers with chemicals and their subsequent conversion into finished products. An historical overview is presented with discussion of the origins of the rubber industry and the developing rubber industry and its occupational health hazards. Manufacturing processes are described for tires, tubes, remolds, and retreads; general rubber goods such as wire and cables, belting, hose, ebonite, rubber footwear, food processing equipment, aircraft deicing equipment, automobile parts; proofed rubber fabrics, adhesives and sealants; and dipped latex products and forms. The chemistry of rubber compounding is reviewed. Exposures in the workplace are discussed with respect to controls, protective equipment, work practices; studies of exposures in the workplace; and biological monitoring. Biological effects include carcinogenic, mutagenic, and teratogenic effects of exposure to accelerators, antioxidants, curing agents; solvents; monomers; talc; carbon blacks; aromatic amines; mineral oils, tar products and polycyclic aromatic hydrocarbons; nitroso compounds; phthalate and adipate esters; and curing fumes and other emissions. Effects in humans other than cancer including dermatologic respiratory, and reproductive, are discussed. Epidemiological studies of carcinogenicity in humans are reviewed: definite associations with cancer of the urinary bladder, lymphatics, stomach, lung, and perhaps, other sites, have been made. (367 Refs)

INDUCTION OF URINARY TRACT CANCER IN ANIMALS

4. RENAL TOXICITY AND TUMORIGENICITY OF HEXACHLOROBENZENE (HCB) IN RATS (R) (MEETING ABSTRACT).

Lambrecht RW, Erturk E, Grunden EE, Headley DB, Peters HA, Morris CR, Bryan GT
Department of Human Oncology and Neurology, University of Wisconsin Center for Health Sciences, Madison, WI, 53792
Proc Am Assoc Cancer Res; 23:210 1982

HCB, a fungicide and by-product of chlorinated hydrocarbon synthesis, has been reported to be a rodent hepatocarcinogen. It was fed to both sexes of R at doses of 0, 200, and 400 ppm for 90 days. On the 91st day, 25/50 R from each group were killed, necropsied, and histologically examined. The remaining 25 R were fed HCB-free diet and were killed at 6-wk intevals thru the 424th day. Growth rate and food consumption were not significantly different between control and test groups except in the final stages of study. In addition to liver neoplasms and generalized lymphatic leukemias, a variety of renal lesions were observed. These included parenchymal degeneration and hyalinous casts (D and C), nephritis and infarcts (N and I), renal cell adenoma (RCA) and carcinoma (RCC). (no Refs)

MODIFICATION OF URINARY TRACT CARCINOGENESIS

5. EFFECT OF SODIUM SACCHARIN ON URINARY BLADDER EPITHELIAL REGENERATIVE HYPERPLASIA FOLLOWING FREEZE ULCERATION (MEETING ABSTRACT).

Murasaki G, Cohen SM
Department of Pathology and Laboratory Medicine, University of Nebraska Medical Center, Omaha, NE, 68105
Proc Am Assoc Cancer Res; 23:218 1982

Long term feeding of sodium saccharin (SAC) induced bladder tumors if administered to rats with a rapidly proliferating bladder epithelium induced by freeze ulceration of cyclophosphamide injection. In this study, we sequentially observed the light and scanning electron microscopic and autoradiographic appearances of regenerative hyperplasia following freeze ulceration of the bladder of male F344 rats, and the effect of SAC on this process when fed as 5% of the diet beginning either immediately or beginning 2 wks after ulceration. Freeze ulceration of the bladder was followed by a marked nodular and papillary hyperplasia appearing around the ulcer with eventual reepithelialization and repair of the ulcer. Nodular and papillary hyperplasia persisted through the 3rd wk after ulceration. The epithelium appeared normal 8 wks after ulceration. The labeling index (LI) of the bladder epithelium 1 hr after 3H-thymidine injection was 10-20% for the first 3 days after ulceration, decreased to 2-3% on day 4, and returned to normal levels 3 wks after ulceration. In rats fed SAC immediately or 2 wks after ulceration, the morphologic and autoradiographic changes were initially similar to the rats with ulceration followed only by control diet, but nodular and papillary hyperplasia persisted through the 8th wk. Although the LI decreased, the rats fed SAC after ulceration maintained the LI at 0.2-0.3% through 8 wks. Control rats without ulceration had normal bladders through 8 wks, but rats fed SAC developed mild simple hyperplasia and slightly increased LI through 8 wks. (no Refs)

6. PROMOTION BY PHENOBARBITAL (PB) OF CARCINOGENESIS INITIATED BY N-[4-(5-NITRO-2-FURYL)-2-THIAZOLYL]FORMAMIDE (FANFT) (MEETING ABSTRACT).

Wang CY, Garner CD, Hirose M
Michigan Cancer Foundation, Detroit, MI, 48201
Proc Am Assoc Cancer Res; 23:403 1982

The present study investigated whether FANFT also initiates liver tumors and PB promotes bladder tumors. Weanling male Fischer rats were divided into 4 groups: I, fed Wayne Lab Blox for 7 wks followed by AIN (American Institute of Nutrition)-76 diet; II, fed the same as I except that the AIN Diet contained 0.05% PB; III, fed Wayne diet containing 0.2% FANFT for 6 wks, followed by 1 wk with Wayne diet, and then by AIN diet; and IV, fed the same as III except that the AIN diet contained 0.05% PB. The experiment was terminated at the end of 93 wks. Rats in III and IV ingested approx 1.2 g FANFT each. The effective number of rats were 27 (I), 24 (II), 40 (III), and 42 (IV), and survival times (wks) were 90 (I); 86 (II); 89 (III); and 87 (IV). The number of rats bearing bladder papillomas and carcinomas, respectively, were 4 and 17 (III), and 4 and 28 (IV). The incidence of bladder carcinomas in IV was significantly greater than in III. Neither I nor II had bladder tumors. The number of rats bearing hepatic cellular-altered foci and neoplastic nodules, respectively, were: 4 and 0 (I); 8 and 1 (II); 7 and 1 (III); and 23 and 6 (IV). The number of hepatic gamma-glutamyltranspeptidase (GGT) foci/cm2 were: 0.12 (I); 1.40 (II); 0.28 (III); and 5.52 (IV) in the rats surviving to the 93rd wk. The number of GGT foci in IV was significantly greater than in the other groups. (no Refs)

7. EFFECTS OF RAT URINE FRACTIONATED BY MOLECULAR WEIGHT ON URINARY BLADDER CARCINOGENESIS (MEETING ABSTRACT).

Oyasu R, Babaya K, Miyata Y
Department of Pathology, Northwestern University Medical School, Chicago, IL, 60611
Proc Am Assoc Cancer Res; 23:404 1982

The present experiment was conducted to determine whether tumor-enhancing activity exhibited by the whole urine resides in a specific fraction(s) when separated by molecular weight. Normal rat urine after preliminary filtration to remove gross debris was filtered through Amicon Diaflo membranes to obtain two types of filtrate, one at an exclusion level of MW 1,000 and the second at an exclusion level of MW 50,000. These filtrates were tested for tumor-enhancing activity in the heterotopically transplanted rat urinary bladders (HTBs) removed from rats pretreated with the carcinogen N-butyl-N-(4-hydroxybutyl)nitrosamine in drinking water for 4 or 10 weeks. The incidences of cancer in HTBs receiving repeated instillations of the filtrate at MW 50,000 did not differ significantly from those of the HTBs receiving whole urine but were significantly higher than those of the HTBs receiving the filtrate at MW 1,000. In the HTBs which had been exposed to the carcinogen for a longer period of time (10 weeks), the filtrate at MW 1,000, enhanced the bladder tumorigenesis over that of the osmolality control. The results indicate that there may be two classes of tumor-enhancing activity: the first and major one being in the fraction above MW 1,000, and a second one being below MW 1,000. The latter fraction appears to exert its effects only on the cells which are in an advanced stage of carcinogenesis. (no Refs)

8. INHIBITION OF CARCINOGENESIS OF THE RAT MAMMARY GLAND AND MOUSE URINARY BLADDER BY A RETINOID AND AN INDUCER OF INTERFERON SYNTHESIS (MEETING ABSTRACT).

McCormick DL, Becci PJ, Moon RC
Illinois Institute of Technology Research Institute, Chicago, IL, 60616
Proc Am Assoc Cancer Res; 23:354 1982

Retinoids are potent inhibitors of chemical carcinogenesis of the mammary gland and urinary bladder in experimental animals. MVE-2 is a divinyl ether-maleic anhydride copolymer which induces interferon synthesis. These studies were conducted to determine the influence on chemical carcinogenesis of combined administration of MVE-2 and the retinoid N-(4-hydroxyphenyl)retinamide (4-HPR). In the mammary study, virgin female Sprague-Dawley rats received a single iv dose of 20 mg N-methyl-N-nitrosourea per kg body weight. In the bladder study, male C57BL/6 x DBA-2 F1 mice received 8 weekly ig doses of 7.5 mg (4-(butylnitrosoamino)-1-butanol). One week after the final carcinogen treatment, animals in both studies were randomized into groups of 50 as follows: (1) placebo diet (2) 4-HPR, 391 mg/kg diet (3) MVE-2, 25 mg/kg body weight, administered ip in 4 week cycles (3 weeks treatment, 1 week rest) throughout the study (4) MVE-2, 12.5 mg,kg, given as above (5) 4-HPR diet + — 25 mg MVE-2/kg (6) 4-HPR diet + 12.5 mg MVE-2/kg. In both studies, 4 HPR (group 2) and the high dose MVE-2 (group 3) treatments re-

sulted in a significant inhibition of carcinogenesis. The low dose of MVE-2 (group 4) was not active in chemoprevention. No synergistic or additive interaction was observed between 4-HPR and MVE-2 at either dose level. These data suggest that either 4-HPR and MVE-2 inhibit carcinogenesis by a common mechanism, or, more likely, that the compounds have an antagonistic activity which precludes an additive or synergistic interaction in cancer inhibition. (no Refs)

BIOCHEMICAL AND METABOLIC ASPECTS IN URINARY TRACT CARCINOGENESIS

9. NICKEL DISTRIBUTION AND DNA LESIONS INDUCED IN RAT TISSUES BY THE CARCINOGEN NICKEL CARBONATE.

Ciccarelli RB, Wetterhahn KE
(c/o Wetterhahn) Dept. Chemistry, Dartmouth Coll., Hanover, New Hampshire, 03755
Cancer Res; 42(9):3544-3549 1982

DNA lesions in nuclei isolated from rat tissues following ip injection of the carcinogen nickel carbonate were measured by the alkaline elution technique. Kidney, liver, lung, and thymus gland nuclei were examined at 3 and 20 hr after treatment for the presence of DNA single-strand breaks and cross-links. Single-strand breaks were detectable in lung and kidney nuclei, and both DNA-protein and DNAS interstrand cross-links were detectable in kidney nuclei. No DNA damage was observed in liver or thymus gland nuclei. A dose response to both single-strand breaks and cross-links was observed in kidney nuclei. Time course studies revealed that maximum DNA damage in kidney nuclei occurred at 2 to 4 hr following injection and also revealed the presence of an active repair process in these nuclei. Repair-resistant DNA-protein cross-links were observed to persist through 48 hr. Tissue and intracellular nickel concentrations as measured by electrothermal atomic absorption spectroscopy were observed to correlate with the levels of DNA damage and repair. A dose response to the concentration of nickel in tissues and nuclei was observed. These results are discussed relative to the solubilization, toxicity, and carcinogenicity of nickel compounds. (Author abstract) (45 Refs)

10. METABOLISM OF BENZO(A)PYRENE AND AFLATOXIN B1 IN CULTURED HUMAN AND ANIMAL MODEL BLADDER AND TRACHEOBRONCHIAL TISSUES (MEETING ABSTRACT).

Daniel FB, Stoner GD, Sandwisch DW, Schenck KM, Schut HA
Health Effects Research Laboratory, U.S. Environmental Protection Agency, Cincinnati, OH, 45268
Proc Am Assoc Cancer Res; 23:327 1982

The metabolism, DNA binding and -adduct formation of benzo(a)pyrene (BP) and aflatoxin B1 (AFB) in human and animal species (monkey, rat, hamster, dog) has been compared using cultured explants of bladder and tracheobronchial tissues. Human bladder and bronchial specimens obtained from autopsies and animal tissues obtained from sacrifice were cultured as explants in serum-free medium. The cultures were rocked to permit intermittent tissue exposure to medium and atmosphere. After three days, the explants were exposed for 24 hrs to either [3H]BP or [3H]AFB (10-6M each). Epithelial cell DNA was isolated by hydroxyapatite chromatography and, after hydrolysis of the DNA, high pressure liquid chromatography (HPLC) was used to identify the carcinogen-DNA adducts. Among the species, BP binding to bladder cell DNA was highest in the human and lowest in the rat and that to tracheobronchial DNA was highest in the hamster and lowest in the dog. For both bladder and tracheobronchial tissues, AFB binding to DNA was highest in the hamster and lowest in the human. In all tissues, 2,3-dihydro-2-(N7-guanyl)-3-hydroxy-AFB and 7,8,9-trihydroxy-10(-N2-deoxyguanosine)-BP adducts were identified after incubation with AFB and BP, respectively. The profile of BP metabolites in the medium (analyzed by HPLC) from all tissues was qualitatively similar. (no Refs)

11. INDUCTION OF ORNITHINE DECARBOXYLASE ACTIVITY IN MOUSE URINARY BLADDER BY L-TRYPTOPHAN AND SOME OF ITS METABOLITES.

Matsushima M, Takano S, Erturk E, Bryan GT
(c/o Bryan) Dept. Human Oncology, Wisconsin Clinical Cancer Center, Univ. Wisconsin Center Health Sciences, 600 Highland Ave., Madison, WI, 53792
Cancer Res; 42(9):3587-3591 1982

The responses of female noninbred mouse urinary bladder ornithine decarboxylase (EC 4.1.1.17) (ODC) and S-adenosyl-L-methionine decarboxylase (EC 4.1.1.50) (SAND) activities to L-tryptophan feeding and to topical intraurethral administration of L-tryptophan and some of its urinary metabolities were studied. Mice fed a diet containing 1% L-tryptophan demonstrated significant increases in vesical ODC and SAMD activities as early as 2 wk after the commencement of the diet. By the end of the 3rd wk, ODC and SAMD activities reached peak values of seven- and three-fold, respectively, significantly greater than the control levels (p less than 0.05 and p less than 0.01, respectively). Then, enzyme activities gradually decreased but remained at levels significantly higher than those of the control mice until the end of the 6th wk when the study was terminated. Topical application by urethral catheter of some urinary tryptophan metabolites was followed by a rapid, transient induction of urinary bladder ODC activity within 5 hr. Statistically significant differences between vehicle controls and xanthurenic acid (p less than 0.01), DL-kynurenine (p less than 0.01), L-kynurenine (p less than 0.01), anthranilic acid (p less than 0.01), and quinaldic acid (p less than 0.05) were observed. However, no significant differences were seen with L-tryptophan, 3-hydroxy-DL-kynurenine, the 8-methyl ether of xanthurenic acid, or D-kynurenine or with 3-hydroxyanthranilic, kynurenic, quinolinic, picolinic, and nicotinic acids. Bladder SAMD was not elevated significantly by most of these directly applied tryptophan metabolites. ODC inducibility by active compounds was followed by mucosal hyperplasia within 7 days. These data suggest that certain L-tryptophan metabolites may be involved in two-stage urinary bladder carcinogenesis in a manner similar to that shown to occur in murine skin tumor systems by other chemicals. (Author abstract) (40 Refs)

MORPHOLOGICAL AND CYTOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

12. CYSTIC NEPHROMA: MORPHOLOGIC SPECTRUM AND IMPLICATIONS.

Gonzalez-Crussi F, Kidd JM, Hernandez RJ
Dept. Pathology, Children's Memorial Hosp., Chicago, IL, 60614
Urology; 20(1):88-93 1982

Among 216 primary renal tumors collected from a pediatric population in metropolitan Chicago, 6 instances corresponded to multiloculated cystic masses conforming to the diagnostic criteria of so-called cystic nephroma. Histopathologically, the component tissues were entirely mature in two cases, but in the remaining four the septa between cysts contained variable amounts of primitive or embryonic tissues; in one of these, a grossly visible mass formed a nodule of typical Wilms tumor. Our experience agrees with previous reports that favor closer structural similarity of these lesions to nephroblastoma than to any known forms of cystic malformation. This concept has important consequences on the therapeutic approach to preoperatively diagnosed multilocular cystic masses of the kidney, and supports the idea that nephrectomy is the treatment of choice. Metastases or local recurrence have not been reported in cases of cystic nephroma. (Author abstract) (18 Refs)

13. IN VITRO CARCINOGENESIS IN CANINE BLADDER (MEETING ABSTRACT).

Klaunig JE, Constantini MG, Barut BA, Goldblatt PJ
Department of Pathology, Medical College of Ohio, Toledo, OH
Lab Invest; 46(1):45A 1982

As part of our overall investigation of mechanisms of bladder carcinogenesis, we have developed methods for establishing primary and secondary cultures of canine bladder urothelial cells. Urinary bladder from adult dogs of mixed breed were removed immediately after exanguination. Four pieces of bladder were placed urothelium side up per 60-mm cultured dish. Two milliliters of Ham's 151 culture medium were added per dish, and dishes were maintained at 36.5 C in a humidified CO2 incubator. Epithelial cells were seen extending from the explants 2 to 3 days after culture initiation. Within 2 to 3 weeks cells were almost confluent on the culture dish. The inclusion of fetal bovine serum in the medium resulted in the overgrowth of epithelial cultures by fibroblasts. The calcium concentration in the medium had a significant influence on differentiation and growth of primary urothelial cells. A concentration of 1 x 10(-4) M calcium appeared optimal for cell growth and prevention of differentiation. Secondary cultures were initiated by trypsinization of primary cultures. Fetal bovine serum was required in the medium for secondary culture cell growth. DNA repair evident in explants, primary, and secondary cultures following exposure to methylnitrosourea aflatoxin B1 4-aminobiphenyl, and benzo(a)pyrene. UDS (unscheduled DNA synthesis) in each compound displayed a linear dose response. Radiolabeled benzo(a)pyrene was metabolized and covalently bound to DNA in bladder explants, primary and secondary cultures. (no Refs)

14. XENOGRAFTS OF HUMAN BLADDER CANCER IN IMMUNE-DEPRIVED MICE.

Kovnat A, Armitage M, Tannock I
(c/o Tannock) Dept. Medicine, Princess Margaret Hosp., Ontario Cancer Inst., Toronto, Ontario, M4X 1K9, Canada
Cancer Res; 42(9):3696-3703 1982

Human bladder cancer from cystoscopic biopsies and from established cell lines was transplanted into mice that were immune suppressed by thymectomy plus sequential treatment with 1-beta-D-arabinofuranosylcytosine and whole-body irradiation. Each of four established human bladder cancer cell lines generated transplantable tumors in these mice, and some of the mice developed pulmonary metastases. Eight of 33 cystoscopically obtained biopsies of transitional cell carcinoma and one from a metastatic site led to xenografts that grew progressively, and some of these have been transplanted and/or have generated cell lines in vitro. Xenografts grew after a lag period of 6 to 32 wk and had doubling times of 9 to 30 days. All of those examined histologically were consistent with transitional cell carcinoma, but some of the xenografts became more or less well differentiated in first and subsequent passages. The immune-deprived mouse is an alternative host to the nude mouse for generation of human tumor xenografts and may be a useful model for study of biological properties and therapeutic response of human bladder cancer. (Author abstract) (23 Refs)

VIRAL AND IMMUNOLOGICAL ASPECTS OF URINARY TRACT CARCINOGENESIS

15. HERPESVIRUSES IN METASTATIC LUCKE RENAL ADENOCARCINOMA.

McKinnell RG, Cunningham WP
Nuffield Dept. Pathology, John Radcliffe Hosp., Headington, Oxford OX3 9DU, England
Differentiation; 22(1):41-46 1982

The etiologic agent of the renal adenocarcinoma of leopard frogs, Rana pipiens, is the Lucke tumor herpesvirus (LTHV). The virus is easily detected with thin section electron microscopy in primary tumors of frogs which have been exposed to a cold environment. Several spontaneous metastatic nodules and a large primary tumor were detected at autopsy of a frog which had been maintained at 4 C for 73 days. LTHV was found not only in the primary tumor, as previously reported, but also was present in metastatic tumor cells in the liver, fat body, and bladder. The presence of LTHV in metastatic cells demonstrates that the differentiated state of primary Lucke tumor cells is retained in its metastatic colonies even at the fine structure level revealed by electron microscopy. (Author abstract) (25 Refs)

16. MACROPHAGE MIGRATION INHIBITION IN PATIENTS WITH RENAL CARCINOMA (MEETING ABSTRACT).

Livni E, Nissenkorn I, Zamir R, Servadio C
Clinical Lab and Department of Urology, Beilinson Hospital, Petah Tiqva, Israel
Proc Am Soc Clin Oncol; 1:C-171 1982

Cell mediated immune(CMI) response towards human tumors was described in a number of human malignancies. This study was undertaken to investigate CMI to renal cell carcino-

ma extracts in patients before undergoing surgery, to find out whether this test might be of diagnostic aid in the differential diagnosis of renal carcinoma and benign cyst. The macrophage migration inhibition factor(MIF) method was used to determine the CMI of 40 patients with renal carcinoma and benign cysts towards renal carcinoma extracts. The MIF test was performed before operation, one week post surgery and 3 months later. Seventy-seven percent of the non-metastatic patients had positive migration indices to one or more of the extracts, before operation, while none of the metastatic cases responded to any of them. Two of the 3 patients without clinically evident metastases and who did not respond to tumor extracts had huge tumors with spread into the perinephric fat and microscopic evidence of invasion into the small blood vessels. None of the 20 patients with renal cysts responded to the tumor extracts. Of the 14 renal carcinoma patients who were examined 1 week post surgery, 10 had a positive response, among them 3 who were unresponsive before operation. Positive migration indices were still found in 8 out of 10 renal carcinoma patients, 3 months after operation. The results favor the use of the MIF technique as an aid in the differential diagnosis of primary renal carcinoma from benign cysts, provided that the malignancy is without metastases. (no Refs)

17. IMMUNOLOGICAL REACTIVITY IN CARCINOMA IN SITU OF THE BLADDER.

Hudemann B, Riedel H, Seyfarth M, Werner H, Erdmann T
Urologische Klinik, Wilhelm-Pieck-Universitat Rostock, Ernst-Heydemann-Strasse, DDR-2500 Rostock, E. Germany
Z Urol Nephrol; 75(4):253-257 1982

In vitro and in vivo immunological reactivities were studied in 13 patients with carcinoma in situ (CIS) of the bladder and in 29 controls. The patients with CIS did not differ from the controls in skin tests using five recall antigens and the primary antigen dinitrofluorobenzene. In electrophoretic tests, 11/13 CIS patients showed a slowing of lymphocyte mobility when the cells were incubated with bladder tumor-associated antigen; 10/13 showed a similar slowing of lymphocyte mobility when human encephalitogenic protein was used as the antigen. The findings suggested that CIS is the first stage in malignant degeneration. (14 Refs) (In GER)

18. NATURAL ANTIBODY TO A HUMAN BLADDER CANCER CELL LINE (MEETING ABSTRACT).

Grossman HB
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

Sera from 144 healthy blood donors were screened for naturally occurring antibody against the bladder carcinoma cell line RT4 using an immune adherence (IA) assay. One hundred twenty-four had no titer at 1/4 dilution; 18 had a titer of 1/4; and one had a titer of 1/16. Only one serum (9241) exhibited high titer with reactivity at a dilution of 1/124. Qualitative and quantitative absorptions were performed with a wide variety of cells to characterize the specificity of the reaction. Aliquots of absorbed serum were tested for residual IA activity on RT4 target cells. Reactivity was absorbed by the bladder carcinomas RT4 and 5637 and the lung carcinoma SK-LC-LL. Antigens related to fetal bovine serum were eliminated because RT4 cells grown in human A positive serum for five passages completely absorbed the activity of serum 9241 for RT4. Other bladder carcinoma cell lines and other malignant cell lines did not abrogate reactivity. Similarly, cultured normal kidney cells, fibroblasts, fetal cells, xenogeneic cells, and Epstein-Barr virus transformed lymphoblasts did not remove reactivity. Non-cultured erythrocytes and three surgically obtained specimens of human urothelium did not absorb reactivity of serum 9241 for RT4. One urothelial specimen from a patient with transitional cell carcinoma of the ureter completely removed reactivity. The antigen defined by serum 9241 for RT4 is heat stable and trypsin resistant as demonstrated by complete absorption with either heated or trypsinized RT4 cells. Quantitative absorption analyses showed that RT4, 5637, and SK-LC-LL present an equal amount of antigen(s) per cell as defined by serum 9241. (no Refs)

19. MONOCLONAL ANTIBODY DU83-21-4 MEDIATES CYTOTOXICITY TO HUMAN PROSTATE AND BLADDER TUMOR CELLS (MEETING ABSTRACT).

Wright GL, Starling JJ, Beckett ML
Eastern Virginia Medical School, Norfolk, VA, 23501
Fed Proc; 41(3):552 1982

The specificity of the monoclonal antibody DU83-21-4, which was generated by fusing spleen cells from Balb/c mice immunized against the prostate adenocarcinoma cell line DU145 and P3x63/Ag8 mouse myeloma cells, was determined by a radioimmunoassay and a membrane immunofluorescent assay. The DU83-21-4 binds to membrane antigens on both prostate and urinary bladder tumor cells but not to 41 other normal and malignant human cell lines and tissues. Further specificity studies suggest DU83-21-4 antibodies do not bind oncodevelopmental markers (CEA (carcinoembryonic antigen), AFP (alpha-fetoprotein)), prostate differentiation markers (PAP, PA), HLA, DR or fibronectin. These antibodies also crossreact with a surface antigen on a human embryonic lung cell line (CMV-Mj-HEL-1) transformed by a cytomegalovirus (CMV) isolated from a human prostate gland, but not to CMV polypeptide antigens or other human cells transformed or infected by CMV virus. The DU83-21-4 antibodies mediate complement-dependent and antibody-dependent cytotoxicity to prostate and bladder tumor cells and the CMV-Mj-HEL-1 cells but not other normal and malignant cells. The crossreactivity of the DU83-21-4 antibody with the CMV transformed line and its reactivity with prostate and bladder tumors may be significant in view of the high incidence of herpes-like viruses with the human urogenital tract. (no Refs)

20. HUMAN BLADDER TUMOR ASSOCIATED SURFACE ANTIGENS (MEETING ABSTRACT).

Sramek SJ, Reichert DF, Smith KO, Lamm DL
No affiliation given
77th Annual Meeting of the American Urological Association, Inc., May 16-20, 1982, Kansas City, Missouri. American Urological Association 254 pp., 1982.

A rabbit antiserum was prepared against the human transitional cell carcinoma cell line T24 to characterize possible tumor associated surface antigens. T24 antiserum demonstrated significant reactivity with human bladder tumor antigens and normal bladder antigens by radioimmunoassay (RIA). After repetitive absorption with a pool of antigens collected from normal urine sediments no reactivity with normal bladder antigens could be detected by RIA. The absorbed rabbit antiserum was tested with T24 labeled by one of two methods. Lactoperoxidase-catalyzed radioiodination of intact cells was used to label surface proteins and metabolic labeling with C14 glucosamine was used to label glycoproteins. The immune complexes were isolated on sepharose-bound staphylococcal protein A and then analyzed by SDS (sodium dodecyl sulfate) polyacry-

lamide gel electrophoresis. The majority of the I-125 radioactivity isolated by the immune serum was distributed in seven peaks with the following molecular weights: 1) 170K; 2) 130K; 3) 120K; 4) 70K; 5) 45K; 6) 42K; 7) less than 30 K. In metabolically-labeled cells, glucosamine radioactivity coincided with peaks 3, 6, and 7. The T24 extract released two proteins from patient immune complexes with a mobility in SDS gle identical to peaks 3 and 5. The rabbit anti-T24 serum appears to identify a family of surface and glycosylated tumor-associated antigens. Two of these antigens may be similar to circulating antigens in immune complexes from patients with transitional cell carcinoma. (no Refs)

21. T24 HUMAN BLADDER CARCINOMA ONCOGENE IS AN ACTIVATED FORM OF THE NORMAL HUMAN HOMOLOGUE OF BALB- AND HARVEY-MSV TRANSFORMING GENES.

Santos E, Tronick SR, Aaronson SA, Pulciani S, Barbacid M
Lab. Cellular and Molecular Biology, NCI, NIH, Bethesda, MD, 20205
Nature; 298(5872):343-347 1982

A transforming gene isolated from T24 human bladder carcinoma cells is closely related to the BALB murine sarcoma virus (MSV) onc gene (v-bas). This transforming gene is localized to a 4.6 kilobase pair (kbp) region and is expressed as a 1.2-kbp polyadenylated transcript, which contains v-bas related sequences. Moreover, antisera known to detect the immunologically related onc gene products of BALB- and Harvey-MSV recognized elevated levels of a related protein in T24 cells. The normal human homologue of v-bas was found to be indistinguishable from the T24 oncogene by heteroduplex and restriction enzyme analysis. These results imply that rather subtle genetic alterations have led to the activation of the normal human homologue of v-bas as a human transforming gene. (Author abstract) (48 Refs)

REVIEWS AND OTHER RELATED STUDIES

22. BLADDER CANCER.

Bonney WW, Prout GR
Veterans Admin. Medical Center, Iowa City, IA
AUA Monogr 1: 357 pp., 1982.

Monographs on urothelial cancer (UC) are presented. Four papers discuss the origins and spread of UC. Individual topics include evolving concepts of the cancer cell, origins of urinary bladder cancer, intravesical dissemination and invasion of urinary bladder cancer, and a longitudinal study of factors associated with recurrence and progression of disease in patients with UC. Six papers discuss diagnosis of UC in the early stages. Diagnostic methods described include urinary tract cytology, analysis and clinical significance of blood group antigens on the cell membrane, analysis of chromosomal aberrations, and scanning electron microscopic (SEM) exfoliative cytology. Basic concepts of tumor immunology are reviewed with reference to UC. Classification and staging of UC is described. Four papers present the heterogeneity, surgical management, and chemotherapy of superficial UC. Five papers discuss invasive UC, including the heterogeneity of invasive UC and surgical, radiation, and enterostomal therapy. Five papers discuss metastatic UC. Topics include surgical and chemotherapeutic approaches to management, nutrition of the patient, and hospice treatment of pain in patients with advanced UC. The experimental design of clinical trials and the validity of reports in therapy of UC are discussed. (697 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. ASBESTOS CARCINOGENESIS: ASBESTOS INTERACTIONS AND EPITHELIAL LESIONS IN CULTURED HUMAN TRACHEOBRONCHIAL TISSUES AND CELLS.
Haugen A, Harris C
Div. Cancer Cause and Prevention, NCI, Bethesda, MD
Recent Results Cancer Res; 82:32-42 1982

2. REVIEW: ORAL CONTRACEPTIVES AND MENOPAUSAL ESTROGENS IN RELATION TO BREAST NEOPLASIA.
Brzezinski A, Schenker JG
Dept. Obstetrics and Gynecology, Hadassah Univ. Hosp., POB 12000, 91120 Jerusalem, Israel
Isr J Med Sci; 18(4):433-438 1982

3. LIVER DISEASES DUE TO HORMONAL CONTRACEPTIVES.
Lie TS
Chirurgische Klinik und Poliklinik, Universitat, Sigmund-Freud-Str. 25, D-5300 Bonn 1, W. Germany
MMW; 124(20):489-494 1982
In GER

RADIATION CARCINOGENESIS

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